UNIVERSITY OF MICHIGAN
JUL 18 1951
MEDICAL LIBRARY

Vol. 4 No. 1 JANUARY, 1950

BRITISH JOURNAL OF SOCIAL MEDICINE

EDITORS

F. A. E. CREW and LANCELOT HOGBEN

WITH THE ASSISTANCE OF

ENID CHARLES
G. P. CROWDEN
T. FERGUSON RODGER
J. A. FRASER ROBERTS
LESLIE J. HARRIS
DONALD HUNTER
J. G. KYD
J. R. MARRACK
T. McKEOWN
P. SARGANT FLORENCE
R. S. F. SCHILLING
S. ZUCKERMAN

W. G. CLARK
C. FRASER BROCKINGTON } Representing the Society of Medical Officers of Health

and the EDITOR of the *British Medical Journal*

CONTENTS

PAGE

The Total Lung Volume and its Subdivisions. A Study in Physiological Norms. I. A. G. W. WHITFIELD, J. A. H. WATERHOUSE and W. MELVILLE ARNOTT 1

Congenital Malformations of the Central Nervous System. II. R. G. RECORD and THOMAS McKEOWN 26

Abstracts 51

Advisory Board 60

LONDON

BRITISH MEDICAL ASSOCIATION

TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) 30s. U.S.A. $5.00 SINGLE NUMBER 7s. 6d.

UNIVERSITY OF MICHIGAN LIBRARIES

NOTICE TO CONTRIBUTORS

THE BRITISH JOURNAL OF SOCIAL MEDICINE is intended for the publication of original work in the field, although not necessarily by authors of British nationality.

As understood by those who are responsible for this Journal, social medicine is that branch of science which is concerned with : (*a*) biological needs, interactions, disabilities, and potentialities of human beings living in social aggregates ; (*b*) numerical, structural, and functional changes of human populations in their biological and medical aspects. To a large extent its methods must necessarily be statistical, involving the use of numerical data obtained either from official sources or from special field investigations, and interpreted in the light of established findings of the laboratory and of the clinic. Social medicine takes within its province the study of all environmental agencies, living and non-living, relevant to health and efficiency, also fertility and population genetics, norms and ranges of variation with respect to individual differences and, finally, investigations directed to the assessment of a regimen of positive health. Such being the definition and scope of social medicine as understood by the editors, it follows that this Journal is not meant to provide a platform for those who wish to present their views concerning the place of social medicine in the organizational set-up of medicine as a whole.

The scope of the Journal and, therefore, the content of social medicine will be illustrated by the nature and diversity of the papers that go to the make-up of the first few numbers. These will also show that the territory claimed by social medicine is not adequately covered by journals that serve the interests of the specialists in such allied subjects as public health and preventive medicine, biometrics, eugenics, and the social sciences.

So far as is possible in these difficult days, this Journal will be published quarterly.

All papers submitted for publication and all other editorial matters should be addressed to one of the editors :

F. A. E. Crew, F.R.S., Usher Institute, Warrender Park Road, Edinburgh.

Lancelot Hogben, F.R.S., Queen Elizabeth Hospital, Birmingham 15.

Alternatively papers may be sent in the first instance to any of those whose names appear in the group on the front cover or to any members of the General Advisory Board.

Papers are accepted on the understanding that they are subject to editorial revision, and that they are contributed to this Journal only.

Adequate reference should be made to previous work on the subject of the paper. A summary of observations and conclusions must be given.

Papers sent for publication must be typewritten on one side of the paper only, with double spacing and with a margin of at least 1½ inches. Illustrations should be used sparingly. Photographs should be printed on glossy paper and should be larger than the size desired for reproduction. Drawings and diagrams should be done in black ink on tracing linen, Bristol board, or stout, white paper. Any lettering on these drawings should be lightly inserted in pencil. The Editors express the hope that contributors will study the conventions of shading and design of charts employed in this and subsequent issues of the Journal with a view to standardizing visual symbols for ready recognition.

References should be arranged according to the Harvard system. If the reference is to a book, the place of publication, the number of the edition and the page number should be given. In the text the year of publication must follow the author's name, more than one paper in any one year being indicated by a small letter (*a*, *b*, *c*) after the date. No numbering of references is necessary. At the end of the paper references should be arranged in the alphabetical order of the authors' names. The reference details should be given as follows: author's name, initials, year of publication (in parentheses), title of periodical (in italics, abbreviated according to the *World List of Scientific Periodicals*), volume number (bold type Arabic numerals), and first page number (ordinary type Arabic numerals), thus :

Buzzard, Farquhar (1943). *Practitioner*, **151**, 129.

Grotjahn, A. (1923). *Soziale Pathologie*, 3rd edit., Springer, Berlin.

Contributors will receive one proof, but it is assumed that all but verbal corrections will have been made in the original manuscript; an allowance at the rate of ten shillings per sheet of sixteen pages is made for alterations in the proof (printer's errors excepted), and contributors will be responsible for any excess.

Fifty reprints of papers will, if desired, be provided free. A limited number of additional reprints at cost price can be supplied if application is made when returning proofs. An estimate of the cost will be given on application to the Publishing Manager, British Medical Association.

Papers which have appeared in THE BRITISH JOURNAL OF SOCIAL MEDICINE remain the property of the Journal, and permission to republish them must be obtained from the editors.

Applications for advertisement space should be addressed to the Advertisement Manager, British Medical Association, Tavistock Square, London, W.C.1.

NOTICE TO SUBSCRIBERS

Subscriptions are payable to the British Medical Association. Address: British Medical Association House, Tavistock Square, London, W.C.1

Brit. J. soc. Med. (1950), **4**, 1-25

THE TOTAL LUNG VOLUME AND ITS SUBDIVISIONS. A STUDY IN PHYSIOLOGICAL NORMS

I. BASIC DATA

BY

A. G. W. WHITFIELD, J. A. H. WATERHOUSE, and W. MELVILLE ARNOTT

From the Departments of Medicine and Medical Statistics, Queen Elizabeth Hospital, University of Birmingham

Many previous workers have published the results of their estimations of the total lung volume and its subdivisions in normal subjects. These are tabulated below in Table I.

It will be seen that Hurtado and his co-workers, and Aslett, D'Arcy Hart, and McMichael are the only two groups who have studied any large number of normal subjects. Lassen, Cournand, and Richards (1937) have pointed out that the method used by the Rochester workers (see Nos. 8-11 in Table I) is somewhat

TABLE I

NUMBER, SEX, AGE RANGE, AND POSTURE OF SUBJECTS STUDIED BY PREVIOUS WORKERS

	Author	Year of publication	No. of subjects		Age range	Posture
			Male	Female		
1	Bohr	1907	9	3	18–50	Standing
2	Rubow	1908	—	8	22–27	Standing
3	Lundsgaard and Van Slyke	1918	11	7	21–38	Standing
4	Lundsgaard and Schierbeck	1923	19	8	19–36	Standing
5	Binger	1923	7	7	Not stated	Sitting
6	Lindhard	1926	8 —	— 6	22–51 23–45	Standing Standing
7	Anthony	1930	9	—	Not stated	Standing, sitting and lying
8	Hurtado and Fray	1933	10	—	Average 23	Sitting and lying
9	Hurtado and Boller ..	1933	50	—	18–30	Lying
10	Hurtado, Fray, Kaltreider, and Brooks	1934	—	50	18–34	Lying
11	Kaltreider, Fray, and Hyde	1938	50	—	38–63	Lying
12	Aslett, D'Arcy Hart, and McMichael	1939	66	—	19–63	Sitting
13	Birath	1944	16	19	18–39	Sitting

UNIVERSITY OF MICHIGAN LIBRARIES

inaccurate because their constantly diminishing spirometric volume precluded the possibility of the alveolar air and the gas in the spirometer ever attaining a uniform mixture. This source of error is maximal when the functional residual air exceeds 3·5 l. The subjects examined by Aslett, D'Arcy Hart, and McMichael were all South Wales coal-miners and are therefore to be regarded as occupationally and ethnologically a special group. Spirometry is being used increasingly in cardio-respiratory physiological research, as an aid to diagnosis and as a guide in treatment of cardio-respiratory dysfunction; there is therefore an obvious need for knowledge of the normal range of the total lung volume and its subdivisions in both sexes at all ages. The object of this paper is to supply this need.

Nomenclature

The diversity of terminology employed by previous workers in this field necessitates a preliminary definition of the following terms as used in this paper (see Fig. 1, opposite).

(*a*) *Resting Respiratory Level.*—A line joining the points reached on a spirogram at the end of each of a series of normal expirations.

(*b*) *Complemental Air.*—The volume of air inspired during a maximal inspiration from the resting respiratory level.

(*c*) *Reserve Air.*—The volume of air expired during a maximal expiration from the resting respiratory level.

(*d*) *Vital Capacity.*—The volume of air expired during a maximal expiration following a maximal inspiration. While this has always been the universally accepted definition, Gilson and Hugh-Jones (1949) have advanced convincing statistical evidence that the average of several attempts affords a more reproducible measurement than the maximum; such, however, would not be a vital capacity within the present concept.*

(*e*) *Functional Residual Air.*—The amount of air remaining in the lungs at the resting respiratory level (i.e. at the end of a normal expiration).

(*f*) *Residual Air.*—The amount of air remaining in the lungs at the end of a maximal expiration.

(*g*) *Total Lung Volume.*—The sum of the vital capacity and residual air or of the complemental and functional residual airs.

Method

(*a*) *Lung Volume Measurements.*—All measurements of the total lung volume and its subdivisions were made with the closed circuit Benedict-Knipping spirometer. The technique employed for the determination of the functional residual air was the constant volume hydrogen dilution method as described by McMichael (1939) except that during the latter part of the investigation helium was used instead of hydrogen.

Corrections for temperature and vapour pressure were applied to the functional

* In normal subjects the vital capacity is usually the same as the sum of the complemental and reserve airs.

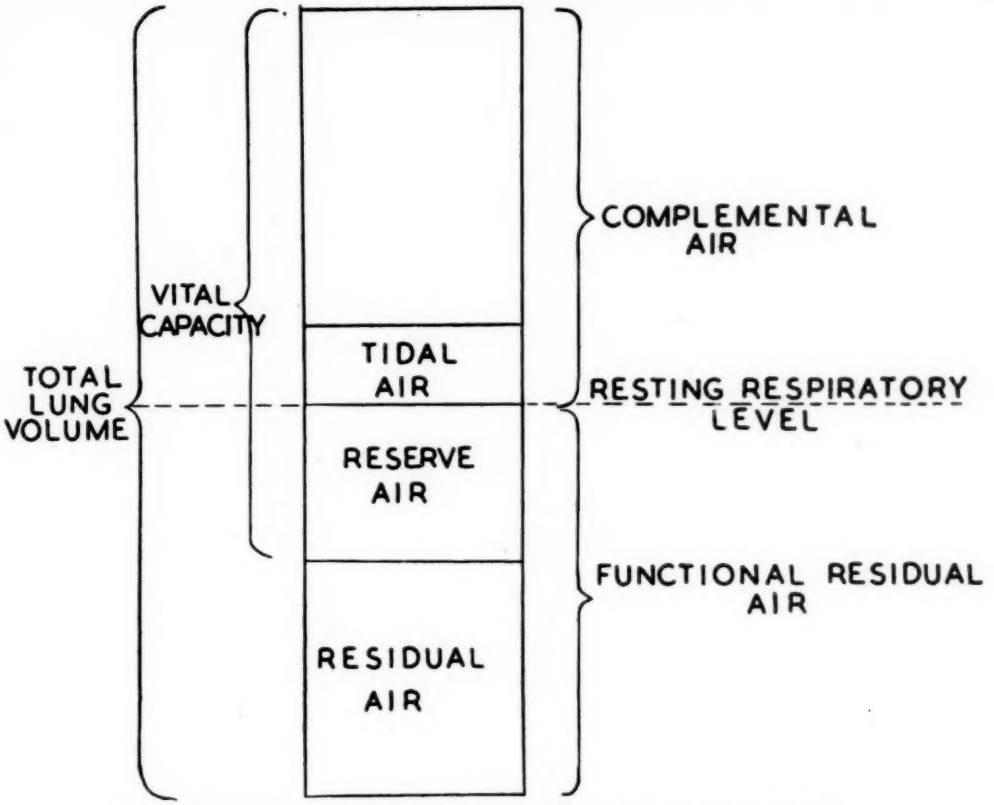

FIG. 1.—Diagram to illustrate definitions of terms as used in this paper.

residual air but not to the vital capacity, complemental, and reserve airs. It has often been suggested that in order to obtain maximum accuracy the vital capacity and its components should be corrected to uniform temperature and vapour pressure but such a procedure involves dubious assumptions.

Probably the only way completely to control these variables would be to use a Benedict-Knipping spirometer (i.e. pump circulated) which, with its connecting tubes, is maintained at 37° C. Our spirometric temperatures fell within the range 16° to 23° C.

(*b*) *Positioning of the Subject.*—Hurtado and Fray (1933b) and McMichael and McGibbon (1939) have pointed out the effect of posture on the total lung volume and its subdivisions. In this investigation all subjects have been examined in the sitting position but a large number have also been examined in recumbency. For sitting examinations the subjects sat " bolt upright " in a chair sufficiently low to allow their feet to rest on the ground, while for lying examinations the subjects lay on a couch with the head supported by one pillow.

(*c*) *Criteria of Normality of Subjects Examined.*—The subjects were drawn from students, staff, and patients at the Queen Elizabeth Hospital, Birmingham. The following criteria of normality were required:

(i) No symptoms or signs of respiratory, cardiac, or haematological disease. (Mild benign hypertensives without cardiac failure were not excluded.)

(ii) No significant previous respiratory, cardiac, or haematological disease. (A remote attack of pneumonia without complications or sequelae did not exclude, but any history of asthma, recurrent bronchitis, or tendency to chest colds was regarded as abnormal.)

(iii) A normal chest radiograph (aortic uncoiling and calcification in older subjects did not exclude).

(iv) A normal blood count and electrocardiogram, though these were not done on all subjects.

The majority of the patients included in this series were suffering from uncomplicated peptic ulcer and none was included whose disability could possibly produce any alterations in their ventilatory capacity.

(*d*) *Scope of the Investigation.*

(i) One highly intelligent and co-operative male subject was examined 27 times in both lying and sitting positions.

(ii) A random sample of the whole group investigated was examined on two occasions in both lying and sitting positions. Three women and sixteen men composed this sample.

(iii) At least ten male subjects in each decennium from 10 to 70 were examined in the sitting position, and of the 64 subjects in this group 41 were also examined in recumbency.

(iv) At least five female subjects in each decennium from 10 to 70 were investigated in the sitting position, and of the 32 subjects in this group 16 were also examined in recumbency.

(*e*) *Selection of Subjects.*—All subjects who satisfied the criteria of normality enumerated above were regarded as eligible for examination. Their degree of co-operativeness and standard of intelligence varied widely and in a few instances much time and patience were required to complete the examination. The only subjects excluded were those whose lack of intelligence or fear made examination impracticable and those whose toothless state made it impossible to prevent leakage around the mouthpiece.

(*f*) *Preparation for Examination.*—Some of the previous workers in this field have carried out their examinations with their subjects under basal conditions. We have not done this, in fact no preparation of any kind was carried out and subjects were examined whenever it was convenient to them and to ourselves.

Results

(*a*) *Repetitive Examination of One Normal Subject.*—A house-physician at the hospital was used for this part of the investigation, which was carried out over a period of four months. It would be impossible to find a more co-operative or better spirometric subject. Full details of his 27 examinations are given at Appendix C (pages 20 and 21), and their statistical analysis in Tables II and III. A table of absolute differences appears at Appendix A (page 19), and a table of ranges at Appendix E (page 24).

From Table II it will be seen that in both lying and sitting positions the standard

TABLE II

ANALYSIS OF RESULTS OF 27 OBSERVATIONS OF ONE SUBJECT

Posture	Division of Lung Volume	Mean (litres)	Coefficient of variation %	Standard deviation of a single observation (litres)	Variance (litres)²
Sitting	Total Lung Volume ..	6·346	3·9	·238	·06158
	Vital Capacity	4·514	2·4	·110	·01202
	Complemental Air ..	2·950	4·2	·125	·01562
	Reserve Air	1·564	8·6	·135	·01828
	Functional Residual Air	3·396	7·4	·253	·06447
	Residual Air	1·832	11·3	·206	·04258
Lying	Total Lung Volume ..	5·959	4·3	·255	·06530
	Vital Capacity	4·150	3·2	·134	·01805
	Complemental Air ..	3·254	3·8	·123	·01515
	Reserve Air	0·896	11·9	·106	·01129
	Functional Residual Air..	2·705	7·9	·214	·04586
	Residual Air	1·809	12·4	·224	·05003

TABLE III

CORRELATION OF DIFFERENCES FROM MEANS (27 OBSERVATIONS OF ONE SUBJECT)

Posture	Division of Lung Volume	Reserve Air	Functional Residual Air	Vital Capacity	Total Lung Volume	Residual Air
Sitting	Complemental Air ..	−·65	−·29	+·09	+·21	+·07
	Reserve Air		+·59	+·49	+·27	+·06
	Functional Residual Air			+·16	+·88	+·85
	Vital Capacity ..				+·60	+·15
	Total Lung Volume ..					+·90
Lying	Complemental Air ..	−·32	+·08	+·66	+·55	+·23
	Reserve Air		+·16	+·50	−·02	−·33
	Functional Residual Air			+·20	+·88	+·88
	Vital Capacity				+·49	−·05
	Total Lung Volume ..					+·85

deviation of a single observation is approximately the same for the vital capacity, complemental air, and reserve air, and amounts to a little over 100 ml. in each instance. Similarly the standard deviations of the total lung volume, functional residual air, and residual air in either posture are all of the order of one fifth to one quarter of a litre.

From this it is clear that the functional residual air is the most variable of the four divisions of lung volume actually measured, the standard deviation of a single observation being approximately double that of the vital capacity and its two components, the complemental and reserve airs. This accords with the impressions gained during the course of the whole investigation. That the relatively high standard deviations of the total lung volume and the residual air are largely a direct result of the high standard deviation of the functional residual air is suggested by the high positive correlation of differences between these three lung volume divisions shown in Table III. Fluctuation of the functional residual air is, however, not the

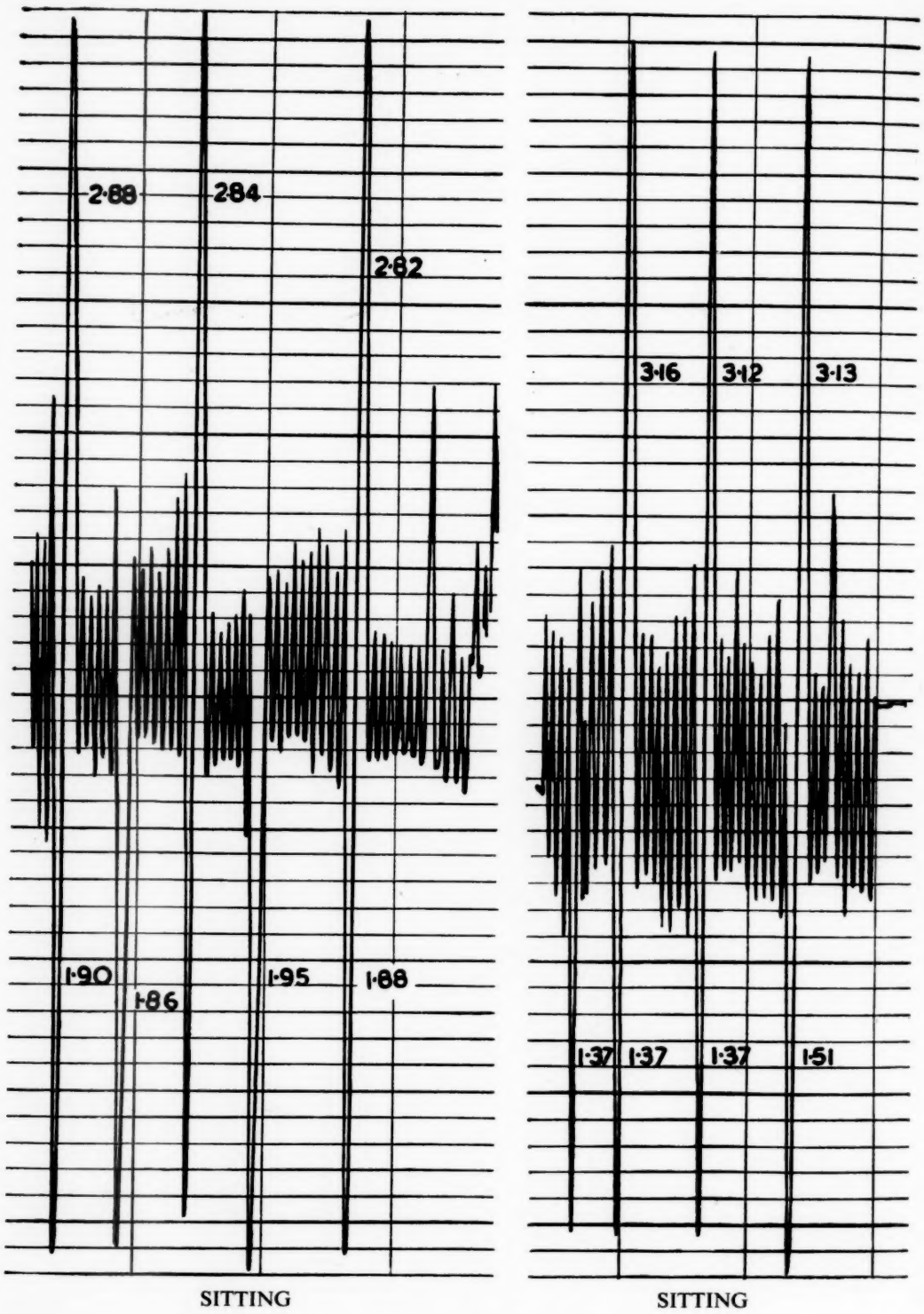

FIG. 2.—Spirograms from the same subject in the same posture showing volitional fluctuation in resting respiratory level.

only factor. It will be noted from Table II that whereas the coefficients of variation of the total lung volume, vital capacity, and complemental air are all low, that of the reserve air is much higher, being of approximately the same order as the coefficients of variation of the functional residual air and of the residual air. It will also be seen from Table III that there is an appreciable negative correlation of differences between complemental air and reserve air. The explanation of these statistical deductions is that the resting respiratory level is to a certain extent under volitional control and may vary as much as half a litre in different tracings on the same individual in the same posture. (See Fig. 2, opposite.)

The first tracing in Fig. 2 shows a vital capacity of 4·78 l. of which 2·88 l. is complemental air and 1·90 l. reserve air. The second tracing shows a vital capacity of 4·64 l. of which complemental air is 3·13 l. and reserve air only 1·51 l. This alteration in the relative proportions of the two components of the vital capacity is clearly seen to be due to a shift in the resting respiratory level.

The effect of this fluctuation in the resting respiratory level is to alter the volume of the reserve air at the expense of the complemental air without affecting the vital capacity. As residual air is calculated by subtracting the volume of the reserve air from that of the functional residual air, any variation of the reserve air will be reflected in the residual air and also, of course, in the total lung volume. Some of the variability of the total lung volume and the residual air is therefore attributable to volitional fluctuations in the resting respiratory level.

(*b*) *Paired Observations on Nineteen Normal Subjects.*—Nineteen subjects, sixteen male and three female, were used for this part of the investigation. In six the second examination was carried out immediately the first had been completed, while in the remaining thirteen a variable period separated the two examinations, the longest interval being 50 days. The detailed results are shown at Appendix D (pages 22 and 23), and their statistical analysis in Tables IV and V. A table of absolute differences is given at Appendix B (page 19) and a table of ranges at Appendix E (page 24).

Tables IV and V show trends similar to those found in the repetitive examination of one subject. The standard deviations of the vital capacity, complemental air, and reserve air are between 100 and 200 ml., while those of the total lung volume, functional residual air, and residual air vary from 200 to 300 ml., again showing that the functional residual air is the most fluctuant of the divisions of lung volume actually measured. That the higher standard deviations of total lung volume and residual air are largely due to the variability of the functional residual air is evident from the high positive correlation of differences between these three divisions of lung volume; and that inconstancy of the resting respiratory level is also a factor is clearly shown by the high negative correlation of differences between complemental and reserve air, and by the relatively higher standard deviation of reserve air when compared with complemental air and vital capacity. The mean differences naturally lead to the same conclusions.

When we began this investigation we felt confident that the accuracy of our

TABLE IV

ANALYSIS OF RESULTS OF PAIRED OBSERVATIONS OF NINETEEN NORMAL SUBJECTS

Posture	Division of Lung Volume	Standard deviation of a single observation (litres)	Variance (litres)²	Mean difference (litres)
Sitting	Total Lung Volume ..	·292	·08587	·345
	Vital Capacity	·101	·01242	·122
	Complemental Air ..	·148	·02180	·156
	Reserve Air	·183	·03359	·200
	Functional Residual Air	·304	·09319	·322
	Residual Air	·250	·06247	·300
Lying	Total Lung Volume ..	·250	·06315	·246
	Vital Capacity	·113	·01288	·130
	Complemental Air ..	·105	·01107	·108
	Reserve Air	·129	·01667	·137
	Functional Residual Air	·213	·04552	·211
	Residual Air	·207	·04289	·210

TABLE V

(19 PAIRED OBSERVATIONS) CORRELATION OF DIFFERENCES FROM MEANS

Posture	Division of Lung Volume	Reserve Air	Functional Residual Air	Vital Capacity	Total Lung Volume	Residual Air
Sitting	Complemental Air ..	−·79	−·10	+·02	+·17	+·46
	Reserve Air		+·57	+·65	+·19	−·03
	Functional Residual Air			+·88	+·88	+·80
	Vital Capacity				+·60	+·36
	Total Lung Volume ..					+·93
Lying	Complemental Air ..	−·55	+·15	+·30	+·54	+·49
	Reserve Air		+·35	+·63	+·07	−·26
	Functional Residual Air			+·53	+·91	+·81
	Vital Capacity				+·58	+·16
	Total Lung Volume ..					+·90

results would depend to a considerable extent on the intelligence and co-operativeness of the subject and on the amount of practice that he had had in the use of the spirometer. That this belief was unfounded is shown by Table VI, which compares the variances of the 27 examinations of one highly intelligent and co-operative subject with those of the nineteen paired observations.

McMichael (1939) carried out 25 paired estimations of the functional residual air in normal subjects in the sitting posture by the same method as that we have used. Previously (Herrald and McMichael, 1938) he had published the results obtained by using a modification of Christie's method (Christie, 1932) in 42 paired observations. A comparative statistical analysis of his two series of results and of our own series of 19 is shown in Table VII (opposite).

It will be seen that McMichael succeeded in obtaining a higher degree of accuracy both from his own method and from his modification of Christie's method than we have been able to achieve. As regards the first series of 42 in which he used his modification of Christie's method, it is possible that his greater accuracy

TABLE VI

COMPARISON OF THE VARIANCES OF 27 OBSERVATIONS OF ONE SUBJECT AND OF 19 PAIRED OBSERVATIONS

Division of Lung Volume	Posture	Variances in (litres)² of 27 observations of one subject (a)	Variances in (litres)² of 19 paired observations (b)	(a) as a percentage of (b)
Complemental Air ..	Sitting	0·01562	0·02180	71·7
	Lying	0·01515	0·01107	136·9
Reserve Air	Sitting	0·01828	0·03359	54·4
	Lying	0·01129	0·01667	67·7
Functional Residual Air	Sitting	0·06447	0·09319	69·2
	Lying	0·04586	0·04552	100·8
Vital Capacity	Sitting	0·01202	0·01242	96·8
	Lying	0·01805	0·01288	140·1
Total Lung Volume ..	Sitting	0·06158	0·08587	71·7
	Lying	0·06530	0·06315	103·4
Residual Air	Sitting	0·04258	0·06247	68·2
	Lying	0·05003	0·04289	116·7

TABLE VII

COMPARISON OF MCMICHAEL'S RESULTS WITH THOSE OBTAINED BY AUTHORS FROM 19 PAIRED OBSERVATIONS

Series of observations	(Sitting) Functional Residual Air		
	Mean difference (litres)	Standard deviation of a single observation (litres)	Range of absolute differences (litres)
McMichael's first series of 42 pairs (modified Christie's method) ..	0·222	0·186	0—0·51
McMichael's second series of 25 pairs	0·136	0·09	Not stated
Authors' series of 19 pairs ..	0·322	0·304	0·03—1·14

may have been partly due to the fact that he was dealing with a selected group as regards race, sex, and occupation; and it is obvious from Table VIII (*a*) and (*b*) (overleaf) that much of our inferior accuracy is due to the very large absolute difference (0·93 and 1·14 of a litre respectively) shown by two of our subjects.

In order to be certain that the nineteen subjects used for paired observations were representative we have compared this sample statistically with the entire group. The details of this analysis, which appear at Appendix F (page 25), show that the nineteen subjects can be so regarded.

TABLE VIII

(*a*) RANGE OF ABSOLUTE DIFFERENCES IN AUTHORS' SERIES OF 19 PAIRED OBSERVATIONS IN SITTING POSTURE (LITRES)

+·03, +·06, +·07, −·11, +·11, −·12,
+·13, +·19, +·21, −·22, −·25, −·35,
−·36, −·36, +·45, −·46, −·57, −·93, +1·14

(*b*) TABLE OF ABSOLUTE DIFFERENCES

Range of absolute difference (ml.)	McMichael's first series of 42 (modified Christie's method)		Authors' series of 19		Authors' repetitive examination of one subject (27 observations)	
	Number	% of total	Number	% of total	Number	% of total
0–99	10	24	3	16	11	42
100–199	8	19	5	26	6	22
200–299	11	26	3	16	5	19
300–399	6	14	3	16	2	7
400–499	6	14	2	11	1	4
500–599	1	2	1	5	2	7
600–699			—	—		
700–799			—	—		
800–899			—	—		
900–999			1	5		
1000–1099			—	—		
1100–1199			1	5		

(*c*) *Examination of Subjects of both Sexes from all Decennia.*—As stated above, 64 males and 32 females, including at least ten males and five females from each decennium from 10 to 70, were examined in the sitting position, 41 of the males and 16 of the females being also examined in recumbency. The statistical analysis of the results is shown in Table IX (opposite).

It will be seen that the total lung volume and all its subdivisions vary within very wide limits in both sexes. Some of the smallest volumes obtained were from subjects in the " 10 to 20 " decennium who had not yet finished growing; but the exclusion of these from the series would not materially narrow the wide range of variability; and indeed, in all but three instances, the smallest volumes in the female series were found in the fifth, sixth or seventh decennia. In both sexes and in both postures, the total lung volume showed the highest, and the vital capacity the next highest, standard deviation, while the reserve air showed the lowest standard deviation. The relative magnitude of the standard deviations of the complemental air, functional residual air, and residual air varied within narrow limits according to sex and posture. In the sitting posture and in recumbency, the mean values for the total lung volume and the vital capacity in males were approximately one litre more than in females, while the mean volumes for the complemental air, reserve air, functional residual air, and residual air were all about half a litre greater in males than in females.

The effect of posture on the total lung volume and its subdivisions will be considered in detail in a separate communication by the present authors, but a glance at Table IX shows that the reserve air, functional residual air, and residual

TABLE IX

ANALYSIS OF RESULTS OF EXAMINATION OF 96 SUBJECTS SITTING AND 57 SUBJECTS IN RECUMBENCY

Sex	Posture	Division of Lung Volume	Range	Mean	Standard deviation	Variance	Coefficient of variation %
MALES	Sitting (64)	Total Lung Volume	2·53–8·12	5·744	1·024	1·0488	17·8
		Vital Capacity ..	1·66–5·58	3·997	0·834	0·6952	20·9
		Complemental Air	1·26–4·53	2·728	0·603	0·3633	22·1
		Reserve Air ..	0·27–2·54	1·269	0·470	0·2206	37·0
		Functional Residual Air	1·27–4·78	3·016	0·773	0·5978	25·6
		Residual Air ..	0·57–3·08	1·747	0·584	0·3406	23·4
	Lying (41)	Total Lung Volume	2·31–7·24	5·485	0·941	0·9036	17·2
		Vital Capacity ..	1·78–5·68	4·032	0·741	0·5632	18·4
		Complemental Air	1·58–4·53	3·027	0·674	0·4545	22·3
		Reserve Air ..	0·20–2·60	1·005	0·395	0·1560	39·3
		Functional Residual Air	0·73–4·39	2·459	0·591	0·3488	24·0
		Residual Air ..	0·53–2·58	1·454	0·590	0·3482	40·6
FEMALES	Sitting (32)	Total Lung Volume	2·65–5·52	4·278	0·726	0·5263	17·0
		Vital Capacity ..	1·72–3·98	2·872	0·556	0·3092	19·4
		Complemental Air	1·42–2·70	1·988	0·355	0·1263	17·9
		Reserve Air ..	0·30–1·58	0·884	0·351	0·1233	39·7
		Functional Residual Air	0·98–3·21	2·291	0·510	0·2622	22·3
		Residual Air ..	0·48–2·38	1·406	0·468	0·2187	33·3
	Lying (16)	Total Lung Volume	3·20–5·31	4·319	0·553	0·3056	12·8
		Vital Capacity ..	2·23–4·12	3·125	0·517	0·2673	16·5
		Complemental Air	1·96–3·10	2·463	0·383	0·1465	15·6
		Reserve Air ..	0·17–1·12	0·663	0·242	0·0585	36·5
		Functional Residual Air	1·24–2·64	1·856	0·458	0·2093	24·7
		Residual Air ..	0·53–2·23	1·194	0·478	0·2286	40·1

air are all greater, and the complemental air less, in the sitting than in the lying position.

The Rochester workers' investigations have shown that when the various divisions of lung volume are expressed as a percentage of total lung volume their range of variability is markedly less than when their absolute values are used. Table X (overleaf) shows the statistical analysis of these percentage values. It will be seen that, with one exception, the coefficients of variation of all divisions of the total lung volume are less when they are calculated as percentages of the total lung volume than when their absolute values are used. Nevertheless, even when the various divisions of lung volume are expressed as percentages of the total lung volume, a high standard deviation still remains and a very wide range of variability is still apparent. When expressed as percentages of the total lung volume, the vital capacity and residual air together must equal 100 per cent., as must also the sum of the complemental air and the functional residual air. This makes it impossible to compare the standard deviations of the percentage figures of the various subdivisions of lung volume in the same way as when their absolute figures were being

TABLE X

ANALYSIS OF DIVISIONS OF TOTAL LUNG VOLUME EXPRESSED AS A PERCENTAGE OF THE TOTAL LUNG VOLUME

Sex	Posture	Division of Lung Volume	Percentage of Total Lung Volume			
			Range %	Mean %	Standard deviation	Coefficient of variation %
MALES	Sitting (64)	Vital Capacity ..	54–88	69·8	8·5	12·1
		Complemental Air	28–75	47·8	8·1	16·9
		Reserve Air ..	5–41	22·0	6·8	30·8
		Functional Residual Air ..	25–72	52·2	8·1	15·5
		Residual Air ..	12–46	30·2	8·5	28·1
	Lying (41)	Vital Capacity ..	60–86	73·6	6·6	9·0
		Complemental Air	28–69	55·0	8·2	15·0
		Reserve Air ..	5–43	18·5	6·6	35·6
		Functional Residual Air ..	31–72	45·0	8·2	18·3
		Residual Air ..	14–40	26·4	6·6	25·0
FEMALES	Sitting (32)	Vital Capacity ..	51–82	67·8	7·9	11·6
		Complemental Air	37–63	47·4	5·7	12·0
		Reserve Air ..	8–33	20·5	7·0	34·0
		Functional Residual Air ..	37–63	52·6	5·7	10·9
		Residual Air ..	18–49	32·2	7·9	24·5
	Lying (16)	Vital Capacity ..	50–85	72·4	9·1	12·5
		Complemental Air	46–69	57·0	6·2	10·9
		Reserve Air ..	4–24	15·4	5·6	36·2
		Functional Residual Air ..	31–54	43·0	6·2	14·4
		Residual Air ..	15–50	27·6	9·1	32·9

considered. Nevertheless, the same tendency for the vital capacity to show the highest and the reserve air the lowest standard deviation is again shown.

That the magnitude of the mean absolute figures for the total lung volume and all its subdivisions is greater in males than in females has been pointed out above. However, a comparison of the four sections of Table X shows that the mean percentage figures for males and females are virtually the same, or, in other words, that though the lung volume is greater in males than in females, there is no basic difference in the ventilatory pattern of the two sexes.

The mean percentage figures confirm the postural effects that were noted when the mean absolute figures were considered. In both sexes the reserve air, functional residual air, and residual air are all greater, and the complemental air less, in the sitting than in the lying position. The percentage figures suggest a tendency for the vital capacity to be increased by recumbency but the degree of change is not statistically significant.

The importance of the Residual Air/Total Lung Volume ratio as an index of ventilatory efficiency has long been appreciated and has been particularly stressed by other workers in this field (Hurtado and Boller, 1933; Kaltreider, Fray, and

Hyde, 1938; Hurtado, Kaltreider, Fray, Brooks, and McCann, 1934; Aslett, D'Arcy Hart, and McMichael, 1939; Meakins and Christie, 1930). The general consensus of opinion appears to be that a Residual Air/Total Lung Volume ratio of over 40 per cent. is suggestive of the presence of emphysema or some other pathological process in the lungs. Our studies, both on normal subjects and on the victims of respiratory disease, confirm the validity of this belief, but we are doubtful whether a ratio of over 40 per cent. can be accepted in clinical practice as proof positive of the presence of disease, since seven of our male subjects and five of our female subjects showed Residual Air/Total Lung Volume ratios of from 41 to 49 per cent. in the sitting position, though all twelve satisfied our criteria of normality and had a good exercise tolerance. It must, however, be pointed out that the majority of them belonged to the older age groups, only two being under 47 and five belonging to the seventh decade. Aslett, D'Arcy Hart, and McMichael encountered similar instances in their series.

(*d*) *Comparison of Results with Results of other Workers.*—We have, of course, been interested to compare our results with those obtained by previous workers; the comparative statistical analysis of mean absolute values is shown in Tables XI (*a*), (*b*), (*c*), and (*d*) and that of mean percentage values in Tables XII (*a*), (*b*), (*c*), and (*d*). Since Bohr, Rubow, Lundsgaard and Van Slyke, Lundsgaard and Schierbeck, and Lindhard all carried out their investigations with their subjects standing, their results have been omitted from this part of our study as we have no comparable figures.

Before proceeding to consider our own mean and absolute percentage values in comparison with those of previous workers, various factors affecting their comparability must be stressed. Firstly, Binger used the Panum (1868) classification of lung volume, in which complemental air, reserve air, and functional residual air are all measured from a point midway between normal expiration and inspiration, and not from the resting respiratory level. In Binger's series, therefore, complemental air only includes one half of the tidal air instead of all of it, and reserve air and functional residual air both include one half of the tidal air instead of none of it. Consequently the only divisions of lung volume from Binger's series that are strictly comparable are total lung volume, vital capacity, and residual air, none of which are affected by this different classification. Secondly, none of the other workers whose results we are comparing with our own used the same method for determining the volume of the functional residual air. In particular, we would again refer to the error in the method used by the Rochester workers, which was pointed out by Lassen and others (1937). Thirdly, the number of subjects studied by both Binger and Anthony was very small compared with our own series, and the ages of their subjects were not stated. Finally, only the group studied by Aslett and others (1939) embraced the wide age range included in our series. Nevertheless, a striking parallelism is seen between our own series of females studied in recumbency and those reported by Hurtado, Fray, Kaltreider, and Brooks (1934), both as regards mean absolute and mean percentage values. A similarity almost as great

TABLE XI

(*a*) MALES SITTING. ABSOLUTE VALUES

Division of Lung Volume	Authors' 64 subjects			Binger's 7 subjects*			Anthony's 8 subjects			Aslett, D'Arcy Hart, and McMichael's 64 subjects			Birath's 16 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Total Lung Volume	5·74	1·02	17·8	6·72	0·90	13·4	5·30	0·86	16·2	5·42	0·84	15·5	6·57	0·61	9·0
Vital Capacity	4·00	0·83	20·9	4·97	0·78	15·7	4·10	0·75	18·3	3·8†	0·55	14·5	5·08	0·48	9·0
Complemental Air	2·73	0·60	22·1	2·74	0·70	25·5	2·76	0·52	18·8	—	—	—	3·39	—	—
Reserve Air	1·27	0·47	37·0	2·23	0·42	18·8	1·35	0·53	39·3	1·32	0·30	22·9	1·69	—	—
Functional Residual Air	3·02	0·77	25·6	3·98	0·69	17·3	2·55	0·71	27·8	2·92	0·60	20·6	3·18	0·45	14·0
Residual Air	1·75	0·58	23·4	1·76	0·29	16·5	1·20	0·23	19·2	1·59	0·50	31·6	1·49	0·23	15·0

* Complemental Air excludes half Tidal Air. Reserve Air includes half Tidal Air. Functional Residual Air (i.e. " Middle Capacity ") includes half Tidal Air.

† 66 subjects.

(*b*) MALES LYING. ABSOLUTE VALUES

Division of Lung Volume	Authors' 41 subjects			Anthony's 7 subjects			Hurtado and Boller's 50 subjects			Kaltreider, Fray, and Hyde's 50 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Total Lung Volume	5·49	0·94	17·2	5·05	1·26	25·0	5·97	0·81	13·6	5·37	0·84	15·7
Vital Capacity	4·03	0·74	18·4	3·89	1·04	26·7	4·78	0·59	12·3	4·07	0·62	15·2
Complemental Air	3·03	0·67	22·3	3·07	0·85	27·7	3·79	0·52	13·7	3·37	0·57	17·0
Reserve Air	1·00	0·40	39·3	0·82	0·28	34·1	0·98	0·26	26·5	0·69	0·31	45·3
Functional Residual Air	2·46	0·59	24·0	1·98	0·56	28·3	2·18	0·50	22·9	2·00	0·50	25·0
Residual Air	1·45	0·59	40·6	1·16	0·31	26·7	1·19	0·35	27·1	1·30	0·41	31·4

is shown between our own group of males in the sitting posture and Aslett, D'Arcy Hart, and McMichael's series (1939). Both the male and female subjects observed by Birath (1944) showed very much higher mean values for total lung volume, vital capacity, complemental air, and reserve air, and lower residual air volumes than our own series. This is, no doubt, largely due to the fact that all Birath's subjects were under 40 years old. Racial factors may also have played some part. Similarly Binger's series showed higher mean vital capacities than the subjects we

TABLE XI

(*c*) FEMALES SITTING. ABSOLUTE VALUES

Division of Lung Volume	Authors' 32 subjects			Binger's 7 subjects*			Birath's 19 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Total Lung Volume	4·28	0·73	17·0	4·74	0·65	13·7	4·79	0·63	13·0
Vital Capacity	2·87	0·56	19·4	3·30	0·55	16·7	3·57	0·44	12·0
Complemental Air	1·99	0·36	17·9	1·74	0·32	18·4	2·57	—	—
Reserve Air	0·88	0·35	39·7	1·56	0·32	20·5	1·00	—	—
Functional Residual Air	2·29	0·51	22·3	3·00	0·42	14·0	2·22	0·49	22·0
Residual Air	1·41	0·47	33·3	1·43	0·23	16·1	1·22	0·25	20·0

* Complemental Air excludes half Tidal Air. Reserve Air includes half Tidal Air. Functional Residual Air (i.e. " Middle Capacity ") includes half Tidal Air.

(*d*) FEMALES LYING. ABSOLUTE VALUES

Division of Lung Volume	Authors' 16 subjects			Hurtado, Fray, Kaltreider, and Brooks's 50 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Total Lung Volume	4·32	0·55	12·8	4·24	0·57	13·5
Vital Capacity	3·13	0·52	16·5	3·14	0·41	13·0
Complemental Air	2·46	0·38	15·6	2·42	0·36	14·8
Reserve Air	0·66	0·24	36·5	0·73	0·19	25·8
Functional Residual Air	1·86	0·46	24·7	1·82	0·39	21·6
Residual Air	1·19	0·48	40·1	1·10	0·30	27·0

studied, and though Binger did not state the ages of his subjects it is likely that this is due to their comparative youth.

Comparison of the results of the Rochester workers with our own series of males examined in recumbency raises several interesting issues. Firstly it is seen that the mean functional residual air of both the younger group studied by Hurtado and Boller (1933) and the older group studied by Kaltreider, Fray, and Hyde (1938) is lower than that of our own series, suggesting that the error of their method pointed out by Lassen and others (1937) cannot be a significant factor in any discrepancy, as it tends to give abnormally high volumes for the functional residual air. Secondly, the higher total lung volume, vital capacity, and complemental air, and the lower functional residual air and residual air in the groups studied by Hurtado and Boller (1933) is no doubt due to the fact that their subjects were all drawn from the 18-30 age-group. Thirdly, when compared with our own series, the higher complemental air, and lower functional residual air and residual air in the older age group studied by Kaltreider, Fray, and Hyde (1938) is surprising when one appreciates that their mean age was 48·2 years.

Tables XI and XII show that in the great majority of instances the standard

TABLE XII

(*a*) MALES SITTING. PERCENTAGE VALUES

Division of Lung Volume	Authors' 64 subjects			Binger's 7 subjects*			Anthony's 8 subjects			Aslett, D'Arcy Hart, and McMichael's 64 subjects			Birath's 16 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Vital Capacity	69·8	8·5	28·1	74	3	25	77	3·7	5	71·0	6·6	9·3	77·3	2·5	3·2
Complemental Air ..	47·8	8·1	16·9	40	6	7	53	8·4	16	—	—	—	51·6	5·0	9·7
Reserve Air ..	22·0	6·8	30·8	34	3	11	25	7·0	28	24·6	5·5	22·4	25·7	—	—
Functional Residual Air ..	52·2	8·1	15·5	60	6	10	47	8·4	18	53·7	6·3	11·7	48·4	5·0	10·0
Residual Air ..	30·2	8·5	28·1	26	3	9	23	3·7	16	29·0	6·6	22·8	22·7	2·5	11·0

* Complemental Air excludes half Tidal Air. Reserve Air includes half Tidal Air. Functional Residual Air (i.e. "Middle Capacity") includes half Tidal Air.

(*b*) MALES LYING. PERCENTAGE VALUES

Division of Lung Volume	Authors' 41 subjects			Anthony's 7 subjects			Hurtado and Boller's 50 subjects			Kaltreider, Fray, and Hyde's 50 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Vital Capacity	73·6	6·6	9·0	77	3·9	5	80·2	4·7	5·8	75·5	5·6	7·2
Complemental Air ..	55·0	8·2	15·0	60	5·8	10	63·9	5·5	8·6	62·5	6·4	10·3
Reserve Air ..	18·5	6·6	35·6	16	3·0	19	16·8	5·9	35·1	13·0	5·3	40·7
Functional Residual Air ..	45·0	8·2	18·3	40	5·8	15	36·2	5·4	14·9	37·7	6·5	17·3
Residual Air ..	26·4	6·6	25·0	23	3·9	17	19·8	4·4	22·2	24·5	5·6	22·8

deviation and coefficient of variation of the various divisions of lung volume is greater in our own series than in any of those published by previous workers. This is no doubt largely a reflection of the wider age range of our subjects.

Our own series show mean absolute values for the total lung volume in the sitting position of 5·74 litres for males and 4·28 litres for females, and a volume in the lying position of 5·49 litres for males and 4·32 litres for females. The difficulties of comparing these figures with the results of other workers have been pointed out above but, when the numerous variable factors in the different series are allowed for, there does not appear to be any wide discrepancy between our series and those previously published.

TABLE XII

(*c*) FEMALES SITTING. PERCENTAGE VALUES

Division of Lung Volume	Authors' 32 subjects			Binger's 7 subjects*			Birath's 19 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Vital Capacity ..	67·8	7·9	24·5	69	4	17	74·5	2·8	3·8
Complemental Air ..	47·4	5·7	12·0	36	3	12	53·7	6·0	11·2
Reserve Air	20·5	7·0	34·0	33	3	11	20·9	—	—
Functional Residual Air	52·6	5·7	10·8	64	3	21	46·3	6·0	13·0
Residual Air	32·2	7·9	24·5	31	4	8	25·5	2·8	11·0

* Complemental Air excludes half Tidal Air. Reserve Air includes half Tidal Air. Functional Residual Air (i.e. " Middle Capacity ") includes half Tidal air.

(*d*) FEMALES LYING. PERCENTAGE VALUES

Division of Lung Volume	Authors' 16 subjects			Hurtado, Fray, Kaltreider, and Brooks's 50 subjects		
	Mean	Standard deviation	Coef. of variation	Mean	Standard deviation	Coef. of variation
Vital Capacity ..	72·4	9·1	12·5	74·1	5·0	6·7
Complemental Air ..	57·0	6·2	10·9	57·0	5·8	10·2
Reserve Air	15·4	5·6	36·2	17·0	3·6	21·2
Functional Residual Air	43·0	6·2	14·4	43·0	5·6	13·0
Residual Air	27·6	9·1	32·9	25·9	5·0	19·3

In the sitting position the vital capacity is about 67½-70 per cent., and the functional residual air about 52¼ per cent., of the total lung volume, while in recumbency the vital capacity rises to 72½-73½ per cent. and the functional residual air falls to 43-45 per cent. of the total lung volume.

The Rochester workers and Aslett, D'Arcy Hart, and McMichael have shown that the lung volume and its subdivisions are significantly correlated with age, and also with certain physical and radiological measurements. This aspect has also been studied in our own series and is the subject of a later communication by the present authors (to be published).

SUMMARY AND CONCLUSIONS

(1) Determination of the total lung volume and its subdivisions was carried out 27 times on one normal subject, and twice in 19 normal subjects, in both sitting and lying postures. Sixty-four normal males and 32 normal females, including ten males and five females from each decennium from 10 to 70 were examined in the sitting position, and 41 of the males and 16 of the females were also examined in recumbency.

(2) The repetitive examination of one normal subject and the 19 paired

observations (sitting and lying) show that the standard deviations of single observations of the functional residual air vary from one-fifth to one-third of a litre. The functional residual air shows the highest standard deviation of all the divisions of lung volume actually measured, and this is reflected in the total lung volume and residual air. Some of the variability of functional residual air results from fluctuation in the resting respiratory level.

(3) The accuracy of results obtained in spirometry is not dependent beyond a certain point upon the intelligence and co-operativeness of the subject, nor upon the amount of practice he has had in the use of the spirometer.

(4) The total lung volume and all its subdivisions vary over a wide range. Their variability is less when they are expressed as percentages of the total lung volume than when their absolute volumes are used.

(5) The mean total lung volume in males is about $5\frac{1}{2}$-$5\frac{3}{4}$ l., and in females about $4\frac{1}{4}$ l.; of this the vital capacity comprises about 70 per cent.

(6) The Residual Air/Total Lung Volume ratio is usually 40 per cent. or less in health, but a small proportion of subjects have ratios up to 50 per cent. in the absence of any clinical or radiological evidence of disease.

(7) The total lung volume and all its subdivisions are greater in the male than in the female, but the basic respiratory pattern of the sexes is the same.

(8) The effect of posture on lung volume is briefly discussed.

(9) The authors' results are compared with those of previous workers.

We wish to express our sincere gratitude to Mr. A. C. Pincock for valuable technical advice and assistance, to Dr. O. P. Gray for allowing us to determine his lung volume on 27 occasions, to Professor Lancelot Hogben for kindly placing the facilities of his department at our disposal, to Dr. G. H. Armitage, who is engaged with us in cardio-respiratory research, for his valuable advice and help, and to Imperial Chemical Industries for a grant towards expenses.

References

Anthony, A. J. (1930). *Dtsch. Arch. klin. Med.*, **167**, 129.
Aslett, E. A., D'Arcy Hart, P., and McMichael, J. (1939). *Proc. roy. Soc. B*, **126**, 502.
Binger, C. A. L. (1923). *J. exp. Med.*, **38**, 445.
Birath, G. (1944). *Acta med. scand. Suppl.*, **154**.
Bohr, C. (1907). *Dtsch. Arch. klin. Med.*, **88**, 385.
Christie, R. V. (1932). *J. clin. Invest.*, **11**, 1099.
Gilson, J. C., and Hugh-Jones, P. (1949). *Clin. Sci.*, **7**, 185.
Herrald, F. J. C., and McMichael, J. (1938). *Proc. roy. Soc., B*, **126**, 491.
Hurtado, A., and Boller, C. (1933). *J. clin. Invest.*, **12**, 793.
———, and Fray, W. W. (1933a). *Ibid.*, **12**, 807.
———, and ——— (1933b). *Ibid.*, **12**, 825.
———, ———, Kaltreider, N. L., and Brooks, W. D. W. (1934). *Ibid.*, **13**, 169.
———, Kaltreider, N. L., Fray, W. W., Brooks, W. D. W., and McCann, W. S. (1934). *Ibid.*, **13**, 1027.
Kaltreider, N. L., Fray, W. W., and Hyde, H. van Z. (1938). *Amer. Rev. Tuberc.*, **27**, 662.
Lassen, H. C. A., Cournand, A., and Richards, D. W. (1937). *J. clin. Invest.*, **16**, 1.
Lindhard, J. (1925). *Skand. Arch. Physiol.*, **47**, 188.
Lundsgaard, C., and Schierbeck, K. (1923). *Acta med. scand.*, **58**, 470.
———, and Van Slyke, D. D. (1918). *J. exp. Med.*, **27**, 65.
McMichael, J. (1939). *Clin. Sci.*, **4**, 167.
———, and McGibbon, J. P. (1939). *Ibid.*, **4**, 175.
Meakins, J. C., and Christie, R. V. (1929-30). *Ann. intern. Med.*, **3**, 423.
Panum, P. L. (1868). *Pflüg. Arch. ges. Physiol.*, **1**, 125 (cited by Hurtado and Boller).
Rubow, V. (1908). *Dtsch. Arch. klin. Med.*, **92**, 255.
Whitfield, A. G. W., Waterhouse, J. A. H., and Arnott, W. M. (further communication to be published).

APPENDICES

APPENDIX A

DISTRIBUTION OF ABSOLUTE DIFFERENCES IN TWENTY-SEVEN OBSERVATIONS OF ONE NORMAL SUBJECT

Differences (ml.)		Divisions of Lung Volume											
		Total Lung Volume		Vital Capacity		Complemental Air		Reserve Air		Functional Residual Air		Residual Air	
		Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying
Mean Difference		177	204	89	100	98	100	108	77	175	157	157	172
Number Showing Difference of	0–99 ..	11	5	14	17	15	14	12	19	11	11	10	10
	100–199 ..	5	9	12	5	9	10	11	6	6	8	9	7
	200–299 ..	6	6	1	5	3	2	4	1	5	2	4	5
	300–399 ..	3	5				1		1	2	4	2	2
	400–499 ..		1							1	1	2	3
	500–599 ..	1								2	1		
	600–699 ..	1											

APPENDIX B

DISTRIBUTION OF ABSOLUTE DIFFERENCES IN PAIRED OBSERVATIONS OF NINETEEN NORMAL SUBJECTS

Differences (ml.)		Divisions of Lung Volume											
		Total Lung Volume		Vital Capacity		Complemental Air		Reserve Air		Functional Residual Air		Residual Air	
		Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying	Sitting	Lying
Number Showing Difference of	0–99 ..	10	9	7	11	5	8	3	6	4	4	4	7
	100–199 ..	5	7	6	4	8	4	5	5	1	8	3	5
	200–299 ..	2	1	4	2	2	5	3	5	5	2	5	1
	300–399 ..	2	2	1	2	1	1	3		3	2	1	4
	400–499 ..					1	1	2	1	2	2	2	1
	500–599 ..					2		1	1	2		2	
	600–699 ..			1								1	
	700–799 ..									1		1	
	800–899 ..												1
	900–999 ..							1	1	1			
	1,000–1,099 ..												
	1,100–1,199 ..							1					
	1,200–1,299 ..										1		

APPEN

Details of Twenty-seven Obser

Number of Experiment		1	2	3	4	5	6	7	8	9	10	11
Sitting	Total Lung Volume	6·37	6·38	6·37	7·02	6·56	6·35	5·80	6·11	6·04	6·12	6·21
	Vital Capacity	4·74	4·46	4·64	4·66	4·49	4·39	4·42	4·39	4·47	4·38	4·51
	V.C./T.L.V. %	75	70	73	66	68	69	76	71	74	72	73
	Complemental Air	2·89	3·14	3·13	3·08	3·04	2·93	3·08	2·93	3·08	2·83	2·91
	C.A./T.L.V. %	45	49	49	44	46	46	53	47	51	46	45
	Reserve Air	1·85	1·32	1·51	1·58	1·45	1·46	1·34	1·46	1·39	1·55	1·60
	R.A./T.L.V. %	30	21	24	22	22	23	23	24	23	26	28
	Functional Residual Air	3·48	3·24	3·24	3·94	3·52	3·42	2·72	3·18	2·96	3·29	3·31
	F.R.A./T.L.V. %	55	51	51	56	54	54	47	53	49	54	55
	Residual Air	1·63	1·92	1·73	2·36	2·07	1·96	1·38	1·72	1·57	1·74	1·71
	Resid. Air/T.L.V. %	25	30	27	34	32	31	24	29	26	28	27
Lying	Total Lung Volume	5·64	5·87	6·23	6·22	6·07	5·99	5·51	5·60	5·85	6·48	5·82
	Vital Capacity	4·24	4·20	4·10	4·12	4·33	4·38	4·19	3·99	3·91	4·20	4·05
	V.C./T.L.V. %	75	71	66	66	71	73	76	71	68	65	69
	Complemental Air	3·30	3·26	3·38	3·46	3·35	3·48	3·28	3·18	3·33	3·28	3·10
	C.A./T.L.V. %	59	56	54	56	55	58	60	57	58	50	53
	Reserve Air	·94	·94	·72	·66	·98	·90	·91	·81	·58	·92	·95
	R.A./T.L.V. %	16	15	12	10	16	15	16	14	10	15	16
	Functional Residual Air	2·34	2·61	2·85	2·76	2·72	2·51	2·23	2·42	2·52	3·20	2·72
	F.R.A./T.L.V. %	41	44	46	44	45	42	40	43	42	50	47
	Residual Air	1·40	1·67	2·13	2·10	1·74	1·61	1·32	1·61	1·94	2·28	1·77
	Resid. Air/T.L.V. %	25	29	34	34	29	27	24	29	32	35	31

DIX C

VATIONS OF ONE NORMAL SUBJECT

12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
6·25	6·63	6·03	6·01	6·61	6·52	6·27	6·45	6·41	6·52	6·41	6·30	6·68	6·29	6·37	6·25
4·58	4·46	4·35	4·39	4·65	4·68	4·48	4·50	4·65	4·61	4·58	4·57	4·51	4·50	4·47	4·35
73	67	72	76	70	72	71	70	73	71	71	73	68	72	70	70
2·81	2·73	2·66	2·89	2·94	3·08	2·74	2·82	2·95	3·03	3·03	3·03	3·02	2·97	2·97	2·95
45	40	44	48	44	47	44	44	46	46	47	48	45	47	47	47
1·77	1·73	1·69	1·50	1·71	1·60	1·74	1·68	1·70	1·58	1·55	1·54	1·49	1·53	1·50	1·40
28	27	28	28	26	25	27	26	27	25	24	25	23	25	23	23
3·44	3·90	3·37	3·12	3·67	3·44	3·53	3·63	3·46	3·49	3·38	3·27	3·66	3·32	3·40	3·30
55	60	56	52	56	53	56	56	54	54	53	52	55	53	53	53
1·67	2·17	1·68	1·62	1·96	1·84	1·79	1·95	1·76	1·91	1·83	1·73	2·17	1·79	1·90	1·90
27	33	28	24	30	28	29	30	27	29	29	27	32	28	30	30
5·73	5·60	5·84	5·81	6·16	6·15	5·91	6·15	6·29	6·21	5·65	5·85	6·11	5·95	5·93	6·16
3·92	4·16	4·13	4·07	4·22	4·14	4·24	4·23	4·22	4·33	3·89	3·95	4·12	4·19	4·13	4·29
68	73	71	70	69	67	72	69	67	70	69	68	67	70	70	70
3·12	3·20	3·16	3·14	3·32	3·30	3·24	3·29	3·25	3·38	2·95	3·15	3·10	3·19	3·18	3·37
54	57	54	54	54	54	55	53	52	54	52	54	51	54	54	55
·80	·96	·97	·93	·90	·84	1·00	·94	·97	·95	·94	·80	1·02	1·00	·95	·92
14	16	17	16	15	13	17	16	15	16	17	14	16	16	16	15
2·61	2·40	2·68	2·67	2·84	2·85	2·67	2·86	3·04	2·83	2·70	2·70	3·01	2·76	2·75	2·79
46	43	46	46	46	46	45	47	48	46	48	46	49	46	46	45
1·81	1·44	1·71	1·74	1·94	2·01	1·67	1·92	2·07	1·88	1·76	1·90	1·99	1·76	1·80	1·87
32	27	29	30	31	33	28	31	33	30	31	32	33	30	30	30

APPEN

DETAILS OF PAIRED OBSERVATIONS

Subject		B.G.		D.G.		F.O.		M.W.		R.G.		D.B.A.		P.B.		R.S.	
Sitting	Total Lung Volume	4·29	5·24	4·72	4·81	3·84	4·02	4·86	4·40	7·27	6·72	6·52	5·74	5·64	5·08	2·53	2·33
	Vital Capacity	3·07	3·42	2·98	2·99	2·78	2·90	3·75	3·43	4·76	4·71	5·30	5·22	3·99	3·91	1·66	1·74
	V.C./T.L.V. %	70	65	63	62	72	72	77	78	65	70	81	91	71	77	66	75
	Complemental Air	2·23	2·04	2·05	1·93	1·66	1·65	2·48	2·37	3·60	2·98	3·66	3·81	2·98	2·78	1·26	1·28
	C.A./T.L.V. %	52	40	43	40	43	41	51	54	50	44	56	66	53	55	50	55
	Reserve Air	·84	1·38	·93	1·06	1·12	1·25	1·27	1·06	1·16	1·73	1·64	1·41	1·01	1·13	·40	·46
	R.A./T.L.V. %	18	25	20	22	29	31	26	24	15	26	25	25	18	22	16	20
	Functional Residual Air	2·06	3·20	2·67	2·88	2·18	2·37	2·38	2·03	3·67	3·74	2·86	1·93	2·66	2·30	1·27	1·05
	F.R.A./T.L.V. %	48	60	57	60	57	59	49	46	50	56	44	34	47	45	50	45
	Residual Air	1·22	1·82	1·74	1·82	1·06	1·12	1·11	·97	2·51	2·01	1·22	·52	1·65	1·17	·87	·59
	Resid. Air/T.L.V. %	30	35	37	38	28	28	23	22	35	30	19	9	29	23	34	25
Lying	Total Lung Volume	4·51	4·76	4·38	4·28	3·90	3·93	4·93	4·95	7·17	5·99	6·03	5·74	4·94	4·46	2·31	2·13
	Vital Capacity	3·21	3·39	2·93	2·89	3·01	2·93	3·79	3·76	4·91	4·57	4·96	5·01	3·98	3·68	1·78	1·91
	V.C./T.L.V. %	71	71	67	68	77	75	77	76	70	76	82	87	81	83	77	90
	Complemental Air	2·60	2·57	2·14	2·11	2·40	2·53	3·01	3·00	3·81	3·51	3·84	4·13	3·05	2·98	1·58	1·60
	C.A./T.L.V. %	58	54	49	49	62	64	61	61	53	59	64	72	62	67	68	75
	Reserve Air	·61	·82	·79	·78	·61	·40	·78	·76	1·10	1·06	1·12	·88	·93	·70	·20	·31
	R.A./T.L.V. %	13	17	18	19	15	11	16	15	17	17	18	15	19	16	9	15
	Functional Residual Air	1·91	2·19	2·24	2·17	1·50	1·40	1·92	1·95	3·38	2·48	2·19	1·61	1·89	1·48	·73	·53
	F.R.A./T.L.V. %	42	46	51	51	38	36	39	39	47	41	36	28	38	33	32	25
	Residual Air	1·30	1·37	1·45	1·39	·89	1·00	1·14	1·19	2·28	1·42	1·07	·73	·96	·78	·53	·22
	Resid. Air/T.L.V. %	29	29	33	32	23	25	23	24	30	24	18	13	19	17	23	10

DIX D

OF NINETEEN NORMAL SUBJECTS

N.M.		H.C.		C.F.		T.D.		G.C.		J.M.A.C.S.		J.F.		E.T.		J.H.		R.C.		W.L.	
6·11	6·37	7·29	7·70	6·81	7·09	7·17	6·85	5·92	5·84	6·77	6·66	5·77	5·48	6·94	6·60	5·16	5·41	5·64	5·72	5·92	6·30
4·74	4·48	5·57	5·60	5·45	5·54	5·58	5·68	4·83	5·01	4·80	4·80	3·63	3·43	4·37	4·32	3·65	3·64	3·23	3·30	4·50	4·63
78	70	76	73	80	78	78	83	82	86	71	72	63	63	63	65	71	67	57	58	76	74
2·80	3·03	3·74	3·70	3·92	3·84	3·55	3·80	3·40	3·43	2·70	2·72	1·61	1·78	3·04	2·95	2·19	2·31	2·30	2·50	2·78	3·10
46	48	51	48	58	54	50	56	57	59	40	41	28	32	44	45	42	43	41	44	47	49
1·94	1·45	1·83	1·90	1·53	1·70	2·03	1·88	1·43	1·58	2·10	2·08	2·02	1·65	1·33	1·37	1·46	1·33	·93	·91	1·72	1·53
32	22	25	25	22	24	28	27	25	27	31	31	35	31	19	20	29	24	16	16	29	25
3·31	3·34	3·55	4·00	2·89	3·25	3·62	3·05	2·52	2·41	4·07	3·94	4·16	3·70	3·90	3·65	2·97	3·10	3·34	3·22	3·14	3·20
54	52	49	52	42	46	50	44	43	41	60	59	72	68	56	55	58	57	59	56	53	51
1·37	1·89	1·72	2·10	1·36	1·55	1·59	1·17	1·09	·83	1·97	1·86	2·14	2·05	2·57	2·28	1·51	1·77	2·41	2·31	1·42	1·67
22	30	24	27	20	22	22	17	18	14	29	28	37	37	37	35	29	33	43	40	24	26
6·24	6·54	7·17	7·32	6·97	6·88	6·46	6·14	5·83	5·65	6·25	5·82	5·25	5·15	6·77	6·58	4·99	5·07	5·36	5·17	5·80	5·70
4·61	4·46	5·68	5·82	5·40	5·55	5·17	5·24	4·51	4·70	4·68	4·40	3·39	3·42	4·31	4·29	3·66	3·75	3·58	3·30	4·53	4·50
74	68	79	80	77	81	80	85	77	83	75	75	65	66	64	65	73	74	67	64	78	79
3·32	3·62	4·53	4·41	4·30	4·35	4·25	4·02	3·70	3·72	3·30	3·15	2·24	2·28	3·17	3·15	2·60	2·64	3·04	2·85	3·59	3·60
53	55	63	60	62	63	66	65	63	66	53	54	43	44	47	47	52	52	57	55	62	63
1·29	·84	1·15	1·41	1·10	1·20	·92	1·22	·81	·98	1·38	1·25	1·15	1·14	1·14	1·14	1·06	1·11	·54	·56	·94	·90
21	13	16	20	15	18	14	20	14	17	22	21	22	22	17	18	21	22	10	11	16	16
2·92	2·92	2·64	2·91	2·67	2·53	2·21	2·12	2·13	1·93	2·95	2·67	3·01	2·87	3·60	3·43	2·39	2·43	2·32	2·32	2·21	2·10
47	45	37	40	38	37	34	35	37	34	47	46	57	56	53	53	48	48	43	45	38	37
1·63	2·08	1·49	1·50	1·57	1·33	1·29	·90	1·32	·95	1·57	1·42	1·86	1·73	2·46	2·29	1·33	1·32	1·78	1·76	1·27	1·20
26	32	21	20	23	19	20	15	23	17	25	25	35	34	36	35	27	26	33	34	22	21

APPENDIX E

TABLE OF RANGES

Series of Experiments		Posture		Division of Lung Volume											
				Total Lung Volume		Vital Capacity		Complemental Air		Reserve Air		Functional Residual Air		Residual Air	
				Max.	Min.	Max.	Min.	Max.	Min.	Max.	Min.	Max.	Min.	Max.	Min.
Twenty-seven Examinations of One Normal Subject		Sitting	Absolute Figures (l.)	7·02	5·80	4·74	4·35	3·14	2·66	1·85	1·32	3·94	2·72	2·36	1·38
			% Total Lung Volume			76	66	53	41	29	21	59	47	34	20
		Lying	Absolute Figures (l.)	6·48	5·51	4·33	3·89	3·48	2·95	1·02	0·58	3·20	2·23	2·28	1·32
			% Total Lung Volume			78	65	61	51	17	10	49	39	35	22
Nineteen Paired Observations	First Determination	Sitting	Absolute Figures (l.)	8·12	2·53	5·58	1·66	3·84	1·26	2·10	0·40	4·50	1·27	3·08	0·83
			% Total Lung Volume			86	57	59	28	44	15	72	41	43	14
		Lying	Absolute Figures (l.)	7·19	2·31	5·68	2·93	4·53	1·58	1·38	0·20	2·95	0·73	2·46	0·53
			% Total Lung Volume			83	64	68	43	22	9	57	32	36	17
	Second Determination	Sitting	Absolute Figures (l.)	8·06	2·33	5·68	1·74	3·92	1·28	2·08	0·46	4·44	1·05	3·02	0·52
			% Total Lung Volume			91	58	66	32	31	16	68	34	40	9
		Lying	Absolute Figures (l.)	7·32	2·13	5·82	1·91	4·41	1·60	1·41	0·31	3·43	0·53	2·29	0·22
			% Total Lung Volume			90	64	75	44	22	11	56	25	35	10

APPENDIX F

SHOWING THAT THE NINETEEN SUBJECTS USED FOR PAIRED OBSERVATIONS CAN BE REGARDED AS A REPRESENTATIVE SAMPLE OF ALL SUBJECTS EXAMINED

Posture	Division of Lung Volume	First Measurement				Mean of both measurements	Mean of all Subjects		Weighted Mean: 16 Males 3 Females
		Mean	Variance	Standard deviation	Coefficient of variation				
					%		64 Males	32 Females	
Sitting	Total Lung Volume	5·756	1·6713	1·293	22·5	5·725	5·744	4·278	5·512
	Vital Capacity	4·153	1·1963	1·094	26·3	4·145	3·997	2·872	3·819
	Complemental Air	2·732	0·6119	0·782	28·6	2·736	2·728	1·988	2·611
	Reserve Air	1·422	0·2272	0·477	33·5	1·409	1·269	0·884	1·208
	Functional Residual Air ..	3·025	0·5692	0·755	24·9	2·989	3·016	2·291	2·901
	Residual Air	1·603	0·2740	0·523	32·7	1·580	1·747	1·406	1·693
							41 Males	16 Females	
Lying	Total Lung Volume	5·524	1·5278	1·236	22·4	5·459	5·485	4·319	5·301
	Vital Capacity	4·125	1·0046	1·003	24·3	4·133	4·032	3·125	3·889
	Complemental Air	3·184	0·6386	0·799	25·1	3·173	3·027	2·463	2·938
	Reserve Air	0·942	0·0867	0·294	31·3	0·960	1·005	0·663	0·951
	Functional Residual Air ..	2·341	0·4473	0·669	28·6	2·286	2·459	1·856	2·363
	Residual Air	1·399	0·2214	0·471	33·6	1·326	1·454	1·194	1·413

Brit. J. soc. Med. (1950), **4**, 26-50

CONGENITAL MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM*

II—MATERNAL REPRODUCTIVE HISTORY AND FAMILIAL INCIDENCE

BY

R. G. RECORD and THOMAS McKEOWN

From the Department of Social Medicine, University of Birmingham

In a previous communication (Record and McKeown, 1949) we described an investigation of 930 consecutive malformations of the central nervous system certified as the causes of stillbirths or of first year deaths in the City of Birmingham in the years 1940-1947. Certain data were available for all these malformations in the Maternity and Child Welfare Department's records; additional information was obtained by home visits from 742 mothers of 755† of the 930 malformations, and from a control group of 742 mothers of 757 of the 892 infants born free from malformation, selected by taking every two hundredth name from the registers of live births and stillbirths for the same years. For a fuller discussion of the material and for an account of the procedure followed in classification of the malformations, we refer the reader to the earlier paper.

The most interesting observations so far recorded in this inquiry concerned the association of age and parity of the mother with the risk of birth of a central nervous malformation. We now make use of the information obtained by field inquiry to compare the malformation series and the control series in respect of the reproductive history of the mother, and the familial incidence of malformations of the central nervous system.

1. Reproductive History of the Mother

The possibility that the uterine environment contributes to the appearance of congenital malformations was first discussed at a time when there was little precise information about the physiology of reproduction in mammals. Mall and his contemporaries were impressed by the high incidence of malformations observed in ectopic pregnancies, but they had few facts to guide them in seeking corroborative evidence of the contribution of the uterus. The work of endocrinologists during the past 30 years has placed at our disposal an acceptable account of the physiology of the pituitary, ovary, uterus, and mammary gland in the oestrous or menstrual cycle, and in pregnancy and lactation. So far there has been neither experimental nor clinical confirmation of the relevance of this knowledge to the problem of

* This research was assisted by a grant from the Birmingham University Students' Social Services' Fund.

† 755 malformed propositi derived from families with 1 malformed propositus, 730; families with 2 malformed propositi, 11; families with 3 malformed propositi, 1. Total, 742.

malformations; but the fact that the different phases of reproductive activity are closely inter-related suggests that if the uterus in which the malformed foetus develops is abnormal, there may be other evidence of abnormality in the history of reproduction. We have therefore examined the histories of mothers in the malformation and control series in respect of (*a*) menstruation, (*b*) age at marriage, (*c*) results of other pregnancies, (*d*) lactation, (*e*) fertility.

The relevant data to which we have access were recorded by interrogation of mothers visited at home, and it is evident that not too much weight can be placed on their accuracy. We have, in fact, restricted the examination to questions in which it was considered that errors of reporting were unlikely to be so great as to obscure gross differences between the two groups.

(*a*) *Menstruation.*—Table I (overleaf) shows that there are no appreciable differences in age at onset, length of cycle, or duration of flow, between mothers in the malformation and control groups. When the three main types of malformation are considered separately, there are also no noteworthy differences in the menstrual history of the mothers.

(*b*) *Age at Marriage.*—Since late conceptions may be associated with late marriages, the examination of age at marriage was suggested by Penrose's report that the risk of birth of a central nervous malformation is associated with high maternal age (Penrose, 1946), a result confirmed in this inquiry for hydrocephalus, but not for anencephalus or spina bifida. There is indeed some evidence that women who give birth to these malformations are on the average a little older than other women when they marry: the mean age at marriage was 23·01 for mothers of malformations, and 22·45 for mothers of controls (difference: $0{\cdot}56 \pm 0{\cdot}20$ years).

It is, of course, evident that the distributions of malformations and controls may differ in respect of the time of marriage, in which case before accepting an age difference it is necessary to satisfy ourselves that there has been no conspicuous increase in the age at marriage in recent years.* Data given by the Registrar-General for England and Wales for the years 1931 to 1946 indicate that on the contrary there has been a slight reduction of the mean age at marriage (Table II, overleaf). It should be noted that our observations for Birmingham are based on fertile marriages only, which may explain a mean age at marriage considerably below the national figure for spinsters. Widows, who are less fertile and older, are excluded.

(*c*) *Results of other Pregnancies.*—It is known that mothers who have given birth to a congenital malformation face a greater than average risk of malformed births in later pregnancies, and this is certainly true of the central nervous group (see Section 2). It has also been reported (Malpas, 1937) that rates of abortion, still-birth, and neonatal death are higher in families which have included malformations

* As mothers of malformations are later shown to be not less fertile than mothers of non-malformed births (see under (*e*)), the fact that primiparity is more common among mothers of malformations (see Part I) suggests that their marriages may be more recent.

TABLE I

MENSTRUAL HISTORY OF MOTHERS OF 755 MALFORMATIONS AND OF 742 CONTROLS

Menstruation	Type of Malformation						Controls	
	Anencephalus No.	Spina Bifida No.	Hydro-cephalus No.	Others No.	Total No.	Total %	No.	%
Age at Onset (years)								
10 and under	4	5	2	0	11	1·5	13	1·8
11	14	17	5	0	36	4·8	44	6·0
12	38	47	9	4	98	13·0	92	12·6
13	68	72	20	8	168	22·4	150	20·5
14	75	83	38	6	202	26·9	203	27·7
15	58	45	23	3	129	17·2	124	16·9
16	31	25	13	1	70	9·3	74	10·1
17	11	8	5	1	25	3·3	23	3·1
18 and over	5	5	2	0	12	1·6	9	1·2
TOTAL	304	307	117	23	751	100	732	100
Age unknown	1	2	1	—	4		10	
Mean	13·9	13·7	14·1	13·7	13·8		13·8	
Length of Cycle (days)								
10–14	1	1	0	0	2	0·3	3	0·4
15–19	6	1	0	0	7	0·9	7	0·9
20–24	28	19	7	1	55	7·3	49	6·6
25–29	233	259	98	20	610	80·8	589	79·5
30–34	25	16	5	2	48	6·4	60	8·1
35–39	5	6	4	0	15	2·0	12	1·6
40+	7	7	4	0	18	2·4	21	2·8
TOTAL	305	309	118	23	755	100	741	100
Length unknown	—	—	—	—	—		1	
Mean	27·8	27·9	28·3	27·7	27·9		28·0	
Duration of Flow (days)								
1–2	10	7	5	1	23	3·1	21	2·8
3–4	90	94	43	11	238	31·7	256	34·5
5–6	135	152	44	7	338	45·0	301	40·6
7–8	60	53	23	4	140	18·6	156	21·1
9–10	7	2	0	0	9	1·2	5	0·7
11–12	0	0	1	0	1	0·1	1	0·1
13–14	0	0	0	0	0	0·0	0	0·0
15+	1	0	1	0	2	0·3	1	0·1
TOTAL	303	308	117	23	751	100	741	100
Duration unknown	2	1	1	—	4		1	
Mean	5·8	5·7	5·6	5·2	5·7		5·7	

of the central nervous system. The fact that these malformations usually lead to the death of the foetus *in utero* or shortly after birth clearly explains at least part of the increased foetal loss. Unfortunately since the causes of abortions are in

TABLE II

MEAN AGE OF SPINSTERS AT MARRIAGE
(England and Wales, 1931–1946)

Year	Age at Marriage	
1931–35	25·53	
1936	25·61	
1937	25·62	
1938	25·58	25·38
1939	25·27	
1940	24·97	
1941	24·80	
1942	24·59	
1943	24·81	24·78
1944	24·84	
1945	24·89	
1946		25·44

general unknown, we are unable to consider whether the foetal loss is greater than could be explained by the high incidence of lethal malformations, and we can only report the dimensions of foetal loss when all known central nervous malformations are excluded. Table III gives this information for anencephalus, spina bifida, and hydrocephalus, and for all the malformations compared with the control series. The abortion rate is much higher for sibs of all these malformations than for sibs of controls; the stillbirth rate is higher for sibs of two malformations

TABLE III

RESULTS OF OTHER PREGNANCIES. (ALL KNOWN MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM ARE EXCLUDED)

	Malformations				All Malformations (a)	Controls (b)	Difference (a)–(b)
	Anencephalus	Spina Bifida	Hydrocephalus	Others			
Live births surviving first year ..	514	591	222	31	1,358	1,244	
Live births dying in first year ..	31	37	12	2	82	77	
Total live births ..	545	628	234	33	1,440	1,321	
Stillbirths	30	14	23	1	68	31	
Total births	575	642	257	34	1,508	1,352	
Abortions ..	76	77	28	5	186	109	
Total conceptions	651	719	285	39	1,694	1,461	
Total foetal and infant loss	137	128	63	8	336	217	
Infant mortality rate per 1,000 live births	56·9	58·9	51·3		56·9	58·3	−1·4± 8·9
Stillbirth rate per 1,000 total births ..	52·2	21·8	89·5		45·1	22·9	+22·2± 6·8
Abortion rate per 1,000 known conceptions	116·7	107·1	98·2		109·8	74·6	+35·2±10·3
Total infant and foetal death rate per 1,000 known conceptions	210·4	178·0	221·1		198·3	148·5	+49·8±13·6

Stillbirth and infant mortality rates for Birmingham (1940-47) were 26·8 and 51·3 respectively. The rates for the controls exhibited in Tables III and IV cannot strictly be compared with the rates for all births.

UNIVERSITY OF MICHIGAN LIBRARIES

(anencephalus and hydrocephalus, but not spina bifida); infant mortality rates are not affected.

The material from Table III was reclassified by birth rank, since the magnitude of the rates is known to be associated with parity. When the rate of foetal and infant loss was standardized by applying the rates in each birth rank for malformations to the numbers in each birth rank for controls, the standardized rate was only slightly higher than the crude rate (198·9 compared with 198·3).

It has been reported (Murphy, 1940) that pregnancies immediately before and after the birth of a malformation are most likely to be disturbed. The sibs were therefore allotted birth rank positions in relation to the propositus: first, second, third, and fourth or earlier positions before the propositus; and first, and second or later positions after the propositus. The same rates of foetal and infant loss were calculated (see Table IV and Figure, opposite). The results suggest that the

TABLE IV

DATA FROM TABLE III REARRANGED IN RELATION TO POSITION OF PROPOSITUS

	Sibs of Malformations						Sibs of Control Propositi					
	Conceptions prior to Propositus				Conceptions subsequent to Propositus		Conceptions prior to Propositus				Conceptions subsequent to Propositus	
	4th+	3rd	2nd	1st	1st	2nd+	4th+	3rd	2nd	1st	1st	2nd+
Live births surviving first year	256	130	190	305	319	158	164	133	238	425	216	68
Live births dying in first year	18	6	8	29	18	3	20	11	15	22	7	2
Total live births ..	274	136	198	334	337	161	184	144	253	447	223	70
Stillbirths	18	5	12	16	15	2	2	3	5	11	6	4
Total births	292	141	210	350	352	163	186	147	258	458	229	74
Abortions	17	13	34	58	36	28	11	11	11	31	31	14
Total conceptions ..	309	154	244	408	388	191	197	158	269	489	260	88
Total foetal and infant loss	53	24	54	103	69	33	33	25	31	64	44	20
Infant mortality rate per 1,000 live births	65·7	44·1	40·4	86·8	53·4	18·6	108·7	76·4	59·3	49·2	31·4	28·6
Stillbirth rate per 1,000 total births ..	61·6	35·5	57·1	45·7	42·6	12·3	10·8	20·4	19·4	24·0	26·2	54·1
Abortion rate per 1,000 known conceptions	55·0	84·4	139·3	142·2	92·8	146·6	55·8	69·6	40·9	63·4	119·2	159·1
Total infant and foetal death rate per 1,000 known conceptions	171·5	155·8	221·3	252·5	177·8	172·8	167·5	158·2	115·2	130·9	169·2	227·3
Difference of total rate from mean ..	−26·9	−42·6	+22·9	+54·1	−20·6	−25·6	+19·0	+9·7	−33·3	−17·6	+20·7	+78·8
S.E. of difference ..	23·54	30·78	28·28	23·59	21·69	29·02	28·19	31·51	21·57	17·87	25·04	45·63

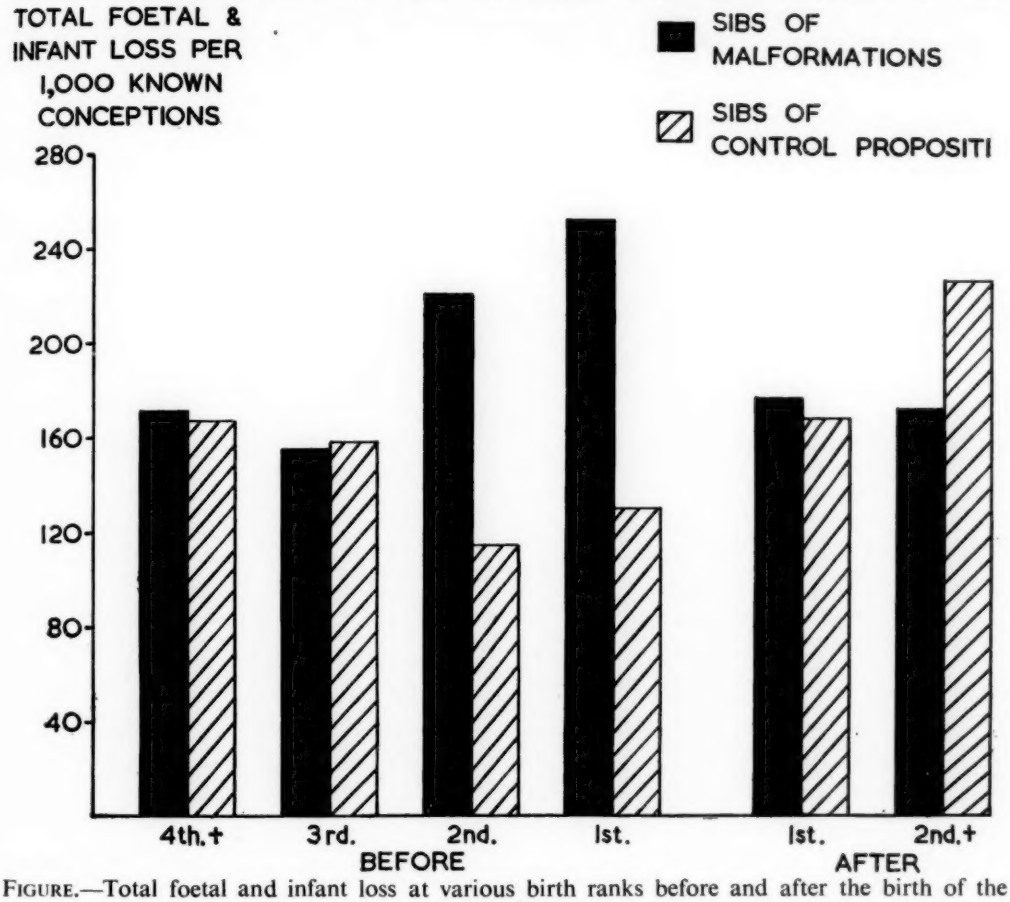

FIGURE.—Total foetal and infant loss at various birth ranks before and after the birth of the propositus.

conception immediately prior to the malformation experiences a greater loss than the others, due to higher rates of infant mortality and abortion, whereas among the control sibs this conception and the one preceding it have the lowest total death rates. The components that make up this loss have diverse trends.

(*d*) *Lactation.*—Enough is known about the physiology of pregnancy and lactation to make it profitable to inquire whether there is any association between the history of breast-feeding and the birth of malformations. It is conceivable that voluntary failure to breast-feed the young might have some later effect on the function of the uterus, or that mothers who give birth to congenital malformations are also less successful in feeding their children.

Our data permit a comparison of the proportions of infants breast-fed for different intervals in the malformation and control groups. The histories are recorded for live births preceding the malformed or control propositus, deaths in the first year of life being excluded. In this context infants are considered breast-fed if they are regularly at the breast, whether or not they also receive some complement of artificial food. Table V gives the information for the malformations and for

TABLE V

DURATION OF BREAST-FEEDING OF SIBS OF MALFORMATIONS AND CONTROLS BORN PRIOR TO THE PROPOSITI*

Duration of Breast-feeding	Sibs of Malformations									Sibs of Control Propositi	
	Anencephalus		Spina Bifida		Hydro-cephalus		Other	All			
	No.	%	No.	%	No.	%	No.	No.†	%	No.†	%
< 2 weeks ..	64	21·4	88	23·2	39	25·3	2	193	22·71	217	22·68
2 weeks— ..	62	20·7	62	16·4	16	10·4	4	144	16·94	194	20·27
3 months— ..	43	14·4	49	12·9	16	10·4	2	110	12·94	145	15·15
6 months and over	130	43·5	180	47·5	83	53·9	10	403	47·41	401	41·90
Total	299	100·0	379	100·0	154	100·0	18	850	100·00	957	100·00

* Deaths in the first year of life are excluded.
† $\chi^2=7·37$ $n=3$ $0·05<P<0·10$

the controls, and exhibits no significant difference between the two distributions. Once again it seemed desirable to examine the data for birth ranks arranged in the order in which they preceded the birth of the propositus. In birth ranks closest to those of the propositi a slight reduction was evident in the proportions of infants breast-fed six months in both the malformation and control series.

The histories of mothers in the control group cannot, of course, be taken as representative of the general population of mothers in respect of the manner of feeding their infants. Records relating to single births, or to deaths in the first year of life are excluded. This may account for the fact that the proportion of children fed at the breast for at least six months is higher than has generally been recorded in this country.

(*e*) *Fertility*.—The fallow periods between consecutive pregnancies of mothers in the malformation and control series were calculated as described below. For this purpose pregnancies resulting in abortions, stillbirths, and live births were included, with exceptions in the case of mothers unmarried at the time of conception.

First births:
(i) The relevant data at our disposal are the age at marriage, the date of the first birth, and the approximate duration of the first gestation in months.
(ii) The date of the first conception was calculated.
(iii) The fallow period was calculated as the number of months between the date of marriage and the estimated date of the first conception.

Later births:
(i) The relevant data at our disposal are the dates of birth of two consecutive pregnancies, and the approximate duration of each gestation in months.
(ii) The date of conception of the second of the pregnancies was calculated.
(iii) The fallow period was calculated as the number of months between the first birth and the estimated date of conception of the second.

The fallow period preceding first conceptions of second marriages was calculated from the date of that marriage.

TABLE VI

MEAN PERIODS OF INFERTILITY (MONTHS) PRECEDING GESTATIONS

Type of malformation	Propositi			Sibs			Mean Size of family (1)+(2) / (1)
	Number of gestations (1)	Sum of fallow periods	Mean fallow period	Number of gestations (2)	Sum of fallow periods	Mean fallow period	
Anencephalus	293	8,916	30·43	632	11,703	18·52	3·16
Spina bifida ..	287	7,448	25·95	688	11,343	16·49	3·40
Hydrocephalus	114	4,252	37·30	268	4,748	17·72	3·35
Other malformations ..	22	771	35·05	39	554	14·21	2·77
All malformations ..	716	21,387	29·87	1,627	28,348	17·42	3·27
Controls ..	710	23,844	33·58	1,338	26,517	19·82	2·88

Table VI gives the mean fallow period in months for the main groups of malformations, and for all malformations compared with controls. The mean is a little shorter for the malformations (29·87 months) than for the controls (33·58 months); the means for the individual malformations vary from 25·95 months for spina bifida to 37·30 months for hydrocephalus.

Table VI also records the same data for sibs of malformations and controls. The most striking feature of the table is that mean fallow periods are uniformly very much lower for sibs than for propositi, an observation which exposes an interesting source of error if the mean fallow period preceding births of malformations is compared with the mean fallow period preceding not-malformed births in the same families.* In this comparison each fraternity usually contributes to one side a single malformation; to the other side it contributes as many sibs as are recorded in the fraternity. It follows that the larger and more fertile the family, the greater is its representation among sibs, whereas its representation among the malformations usually remains unchanged at one. This source of error led Murphy (1940) to the conclusion that the birth of the malformed child was preceded by a period of relative sterility, a suggestion made earlier by Still (1927). Size of family also clearly affects the mean fallow period preceding births of sibs of the individual malformations; for example, if the mean size of family is smaller for anencephalus than for spina bifida, relatively fewer sibs are recorded from the smaller and less fertile families of anencephalics. It has therefore been necessary to examine the mean size of family, which is readily obtained by dividing the total number of births (propositi and sibs) by the total number of propositi. There are in fact slight differences in family size between the different malformations, and between the malformations and the controls.

We must now consider whether the mean fallow period is affected by birth rank. Table VII (overleaf) gives the data by birth rank for malformed and control propositi,

* This situation arises when no control group of births free of malformations is available for comparison.

TABLE VII

MEAN PERIODS OF INFERTILITY (MONTHS) PRECEDING GESTATIONS. DATA ARRANGED IN ORDER OF BIRTHS

Type of Malformation		Order of Birth												Total	
		1		2		3		4		5 and 6		7 and over			
		No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period	No. Gestations	Mean Fallow Period
Anencephalus	Pre-propositi	136	15·15	88	23·53	57	19·42	40	23·83	42	18·19	28	15·46	391	18·90
	Propositi	134	26·43	69	37·96	29	34·62	21	38·52	24	22·75	16	24·81	293	30·43
	Post-propositi	—	—	92	17·79	69	19·61	37	17·27	29	16·21	14	15·43	241	17·90
	Total	270	20·74	249	25·41	155	22·35	98	24·50	95	18·74	58	18·03	925	22·29
Spina bifida	Pre-propositi	138	11·22	103	19·81	61	20·41	39	19·62	45	16·38	42	16·90	428	16·46
	Propositi	121	19·32	60	34·90	43	25·93	23	36·52	19	30·37	21	23·05	287	25·95
	Post-propositi	—	—	86	17·06	70	17·04	40	15·90	37	18·30	27	12·04	260	16·53
	Total	259	15·00	249	22·49	174	20·42	102	21·97	101	19·71	90	16·88	975	19·27
Hydrocephalus	Pre-propositi	59	10·32	48	19·33	28	25·61	21	22·00	21	24·33	15	17·60	192	18·18
	Propositi	40	26·80	29	49·31	16	34·25	8	57·75	12	42·50	9	25·56	114	37·30
	Post-propositi	—	—	26	15·46	25	17·20	12	18·67	8	16·88	5	13·20	76	16·54
	Total	99	16·98	103	26·80	69	24·57	41	28·00	41	28·20	29	19·31	382	23·56
Other malformations	Pre-propositi	12		2		2		1		2		1		20	13·15
	Propositi	7		12		1		1		—		1		22	35·05
	Post-propositi	—		7		10		2		—		—		19	15·32
	Total	19		21		13		4		2		2		61	21·72
Total malformations	Pre-propositi	345	12·65	241	21·19	148	20·86	101	21·68	110	18·36	86	16·49	1,031	17·64
	Propositi	302	23·62	170	39·16	89	29·97	53	40·57	55	29·69	47	24·36	716	29·87
	Post-propositi	—	—	211	17·16	174	18·04	91	16·63	74	17·32	46	13·20	596	17·05
	Total	647	17·77	622	24·73	411	21·64	245	23·89	239	20·65	179	17·71	2,343	21·23
Controls	Pre-propositi	416	13·79	251	22·33	147	22·42	77	26·82	65	22·31	30	16·30	986	18·91
	Propositi	230	25·66	216	38·88	109	37·49	72	37·33	61	37·48	22	22·00	710	33·58
	Post-propositi	—	—	110	27·47	98	20·03	59	21·86	54	19·65	31	17·39	352	22·37
	Total	646	18·02	577	29·51	354	26·40	208	29·05	180	26·65	83	18·22	2,048	24·59

as well as for gestations preceding and following these births. The data again direct attention to the error of a comparison between propositi and all their sibs.

TABLE VIII

STANDARDIZED MEAN PERIODS OF INFERTILITY* (MONTHS) PRECEDING GESTATIONS

Type of Malformation	Propositi		Sibs		(a)÷(b)
	Number of gestations	Standardized mean fallow period (a)	Number of gestations	Standardized mean fallow period (b)	
Anencephalus	293	32·05	632	18·53	1·73
Spina bifida	287	27·88	688	16·12	1·73
Hydrocephalus	114	39·24	268	16·83	2·33
Other malformations ..	22	—	39	—	—
All malformations.. ..	716	31·59	1,627	17·18	1·84
Controls	710	33·58	1,338	19·82	1·69

* Mean periods of infertility for each malformation were standardized by applying the crude means to the numbers of controls in corresponding birth ranks.

Before proceeding to consideration of the effect of parity, we may also note that the fallow period is shorter for pregnancies following than for pregnancies preceding the malformations, which suggests that women who have given birth to a malformation are not deterred from further reproduction. In both the malformation and control series the mean fallow period is considerably shorter for first births, and for births after the sixth, and it is clearly desirable to standardize the results for birth rank before comparing mean fallow periods for all births. Table VIII shows standardized mean fallow periods for each malformation, obtained by applying the crude means to the numbers of controls in corresponding birth ranks. The mean fallow periods for the malformed propositi are slightly increased by this treatment.

A rough index of the fertility of women before the birth of a propositus relative to their fertility before other births, is given by the ratio of the mean fallow periods shown in Table VIII. This ratio is slightly higher for all malformations (1·84) than for controls (1·69), but is distinctly higher in the case of hydrocephalus (2·33). It was thought worth repeating this calculation after excluding first births, and when this was done the ratio for all the malformations was unchanged (1·84) and was higher than for the controls (1·66). The ratio for hydrocephalus was again distinctly raised (2·29). A further refinement was added by exclusion of pregnancies immediately following abortions, since it is reasonable to suppose that the period of infertility which follows will in general be shorter than after notified births, and since abortion is more common in families which include a malformation. The effects already noted were only slightly accentuated by this treatment. On this evidence there is little to suggest that women who give birth to malformations are less fertile than other mothers, or that malformations arise when births succeed each other too rapidly. There is some evidence, especially in the case of hydrocephalus, that women are slightly less fertile in the period preceding the birth of a malformation than in the period which precedes their other conceptions.

In view of the disrupting effect of the war on family life during the greater part of the period in which the births in this series occurred, a discussion on birth spacing would not be complete without reference to the periods of absence of the husband. The available data distinguished between service overseas in which home leave was rare, and service in Great Britain with occasional opportunity for cohabitation of husband and wife, but for simplification of the analysis both categories were considered together, absences for brief periods being disregarded. The data permitted a classification of all legitimate births into three groups: (*a*) families in which the father was absent during the year of birth of the propositus or during the preceding year; (*b*) families in which the father was not absent during the above period but was absent at some other time; (*c*) families in which the father was never absent. As might be expected, the results showed considerable variation with parity; when standardized for this variable they revealed no material differences between the malformation and control groups.

Although it is only remotely connected with the period of infertility, we may consider here the question of age differences between father and mother. On the average fathers were older than mothers by 2·4 years in the case of malformations, and by 2·9 years in the case of controls (difference: $0 \cdot 5 \pm 0 \cdot 2$). We have no reason to stress the importance of a difference of this magnitude, and it will be recalled that mothers of malformations were slightly older at marriage than other mothers. Murphy (1940) also examined this question and observed no significant difference.

2. Familial Incidence of Malformations

(*a*) *Malformations in Fraternities.*—Appendix A (see p. 45) gives details of fraternities in the malformation group in which at least one other malformation among sibs was reported by the mother. We were unable to check the diagnoses of abortions (which are excluded from the analysis), but all diagnoses of stillborn and live born malformations in Birmingham were confirmed in central records for the years after 1936. The fraternities were arranged in three groups. Groups I and II include those in which other malformations involved the central nervous system and resulted in stillbirth or infant death, and Group III includes those in which other malformations were not of the central nervous system or did not lead to stillbirth or infant death.

Group I (12 fraternities). All the malformations (25) occurred in Birmingham in the years 1940-47, and all are in consequence included in the series of 755 malformed propositi.

Group II (16 fraternities). Only one malformation in each fraternity is included in the series of 755 malformed propositi. The other malformations were born outside the city, or outside the period 1940-47.

Group III (6 fraternities).

Appendix B (see p. 49) gives details of fraternities in the control group in which malformations among sibs were reported by the mother. It should be remembered that the controls were selected in such a way that lethal malformations of the

TABLE IX

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM AMONG ALL SIBS OF MALFORMED AND CONTROL PROPOSITI

Group	Fraternities	Total Number* of Offspring	Propositi	Sibs of 742 Propositi	Number of Central Nervous Malformations among Sibs	Percentage of Sibs with Malformations of Central Nervous System
Malformations	742	2,276	742†	1,534	29	(a) 1·89
Controls	742	2,117	742	1,375	4	(b) 0·29

Difference between percentages, (a) $-$(b) $=1\cdot60\pm0\cdot39$

* Includes all notified live births and stillbirths, but excludes abortions.

† Includes only one malformed propositus from each fraternity. The 755 malformed propositi born in the years 1940-47 were derived from: Families with 1 malformed propositus .. 730; ,, ,, 2 ,, propositi .. 11; ,, ,, 3 ,, ,, .. 1 } 742

Thirteen malformed propositi are here entered as sibs.

nervous system were excluded (Part I, Section 3). Only two of the control propositi had other and minor deformities. In one case (l, see p. 49) the second pregnancy resulted in an anencephalic stillbirth, and the fraternity is therefore included in both malformation and control series. In Part I it was estimated that 0·59 per cent. of all infants born in Birmingham in the years 1940-47 had malformations of the nervous system which resulted in stillbirths or infant deaths. Table IX shows that 1·89 per cent. of sibs of the malformed propositi are similarly affected, compared with 0·29 per cent. of sibs of the non-malformed control births. That is to say, the risk of birth of another central nervous malformation among sibs in the first case is about three times the average risk for all families, and in the second case is about

TABLE X

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM AMONG ALL SIBS OF MALFORMATIONS OF DIFFERENT TYPES

	Type of First Malformation				Total
	Anencephalus	Spina Bifida	Hydrocephalus	Other	
Number of fraternities†	302	300	116	23	741*
Sibs of 741 propositi	582	654	260	36	1,532
Number of central nervous malformations among sibs	6	18	3	1	28
Percentage of sibs with malformations of the central nervous system	1·03	2·75	1·15	—	1·83

* One fraternity (Appendix A, Group I, Fraternity "1") in which two twins had hydrocephalus is excluded from this and from subsequent tables. This explains the slight difference between Tables IX and X in the total percentages affected.

† This also gives the number of propositi here considered, since only one is entered from each fraternity.

TABLE XI

THE RELATIVE RISK OF RECURRENCE OF ANOTHER MALFORMATION OF THE SAME OR OF A DIFFERENT TYPE

Sibs of 741 propositi		Type of First Malformation											Total		
		Anencephalus			Spina Bifida			Hydrocephalus			Other				
		582			654			260			36		1,532		
Type of Subsequent Malformation	General Frequency in B'ham (1940-47) per 100 Births	Actual No. (a)	Expected No. (b)	(a) ÷ (b)	Actual No. (a)	Expected No. (b)	(a) ÷ (b)	Actual No. (a)	Expected No. (b)	(a) ÷ (b)	Actual No.	Expected No.	Actual No. (a)	Expected No. (b)	(a) ÷ (b)
Anencephalus	0·23	3	1·35	2·2	7	1·51	4·6	1	0·60	1·7	0	0·08	11	3·54	3·1
Spina bifida	0·25	2	1·43	1·4	10	1·61	6·2	1	0·64	1·6	0	0·09	13	3·76	3·5
Hydrocephalus	0·09	1	0·55	1·8	1	0·62	1·6	1	0·25	4·1	0	0·03	3	1·45	2·1
Other malformations	0·02	0	0·09		0	0·10		0	0·04		1	0·01	1	0·24	
Total	0·59	6	3·42	1·8	18	3·84	4·7	3	1·53	2·0	1	0·21	28	9·00	3·1

When the three main types are considered together the risk of recurrence of the same malformation is given by the ratio $\frac{14}{3{\cdot}21} = 4{\cdot}4$; and the risk of a different malformation by the ratio $\frac{13}{5{\cdot}35} = 2{\cdot}4$.

half. Table X shows that the risk is relatively greatest for spina bifida (2·75 per cent.) and least for anencephalus (1·03 per cent.).

Where one malformation of the central nervous system has been recorded, it is of interest to know the relative risk of recurrence of another malformation of the same or of a different type. This information is contained in Table XI, in which the frequency of each malformation in Birmingham (see Part I, Table XIV) in the years 1940-47 has been used to calculate an expected number for comparison with the actual number observed. Two conclusions may be drawn for each of the three main central nervous malformations: (i) the risk of recurrence of the same malformation is greater than the risk of a different one; (ii) the risk of a different malformation is greater than the risk experienced by the general population of mothers.

When the three main types are considered together, the ratio of the actual to the expected rate of recurrence is 4·4 for the same malformation, and 2·4 for a different malformation.

We have so far considered only the risk of birth of a malformation for *all* sibs born *before* or *after* a propositus. In practice, however, the doctor is required to comment on the likelihood of recurrence *after* a malformation has been born, and this risk is assessed in Table XII (opposite). The data suggest that the risk of recurrence in subsequent sibs is about 1 in 20, almost nine times the risk in the general population of mothers. The risk is greatest where the earlier malformation is spina bifida. Moreover, it will be recalled that two of the three main groups

TABLE XII

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM AMONG SIBS BORN AFTER A MALFORMATION HAS BEEN RECORDED

	Type of First Malformation				Total
	Anencephalus	Spina Bifida	Hydrocephalus	Other	
Sibs born after the first malformation ..	214	247	65	15	541
Number of malformations	6	18	3	1	28
Malformation rate (per cent.)	2·80	7·29	4·62	—	5·18
Number of times by which these rates exceed the rate for Birmingham, 1940–47 (0·59%)	4·8	12·4	7·9		8·8

of central nervous malformations are commonest among first births and are therefore less common in births after the first than in all births. It follows that the comparison with the general population of mothers (as above) understates the relative risk for births after a malformation.

Finally we have used the information recorded in Appendix A (Group III) to obtain the incidence of other major malformations.* There were three of these (pyloric stenosis, imperforate anus, and congenital defect of the heart) among 1,505 sibs of malformations, giving a percentage incidence of 0·2. Among 2,112 sibs of controls there were nine major malformations (Appendix B) when those of the central nervous group (four plus one unspecified) were excluded, giving a percentage incidence of 0·43. The difference between the results for the two series is 0·23 per cent. $\pm$0·19.

The literature contains a number of references to fraternities in which two or more malformations occurred. For malformations in general, including those for which genetic theory gives a satisfactory explanation, Macklin (1936) found a high rate of recurrence in a sibship. Murphy (1940) calculated that malformations affected one sib in every eight born subsequent to a malformation. In almost half of the fraternities in which a malformation recurred, the second malformation was identical with the first. It is noteworthy that in the forty fraternities which experienced a recurrence, 52 of the 91 malformations were defects of the central nervous system. Penrose (1939) records that among 1,041 sibs of malformations, there were 24 with congenital defect (2·31 per cent.). Included in this series was a group of 137 central nervous malformations, having 454 sibs of which ten were malformed (2·20 per cent.). The incidence of central nervous malformations among these 454 sibs was 1·54 per cent.

* Other major malformations here referred to are those (not involving the nervous system) which produce obvious disability at an early age, but do not necessarily lead to death. Other major malformations coexisting with central nervous defects in the same individual are excluded.

TABLE XIII

NUMBERS OF RELATIVES WHO WERE MALFORMED (SIBS EXCLUDED)

Type of Malformation of Propositus*	No. of Fraternities	Type of Malformation of Relative											Total Number of Malformed Relatives
		Central Nervous System					Others Specified						
		Anencephalus	Spina Bifida	Hydrocephalus	Others	Total	Special Senses	Hare-lip and/or Cleft Palate	Extremities	Others	Total	Unspecified	
Anencephalus	302	6	8	1	1	16	4	4	5	—	13	5	34
Spina bifida ..	300	4	9	4	—	17	2	8	4	3	17	4	38
Hydrocephalus	117	—	3	—	—	3	—	2	—	—	2	1	6
Other malformations ..	23	—	1	—	—	1	—	1	—	—	1	—	2
Total	742	10	21	5	1	37	6	15	9	3	33	10	80
Controls ..	742	1	6	2	1	10	3	0	9	3	15	3	28

* Where more than one malformed propositus was recorded in a fraternity, the type of the first born was used for this classification.

Cases of recurrence of anencephaly in a sibship are not infrequent in the literature. Dunn and Salter (1944) quote ten references to this phenomenon and record a case which they observed where two successive foetuses in a sibship had anencephalus with spina bifida. A further case was reported by Quigley (1943). Among authors reporting recurrence of spina bifida are Pybus (1921) and Hindse-Nielsen (1938). In the latter's series, the propositi had 548 sibs of whom 28 (5·1 per cent.) showed spina bifida aperta. Recurrence of hydrocephalus appears to be less commonly recorded. No mention of it was made in the 58 cases reported by Malpas (1937) or in the 43 cases published by Penrose (1939). Butler-Smythe (1889) reported one fraternity in which three children had hydrocephalus with spina bifida and the remaining two had abnormally large heads. Recurrence of hydrocephalus was noted in seven fraternities in the series published by Murphy (1940). Recurrence of central nervous malformations has also been reported in the litters of experimental animals (Snell and Picken, 1935; J. Hammond quoted by Boyd, 1942).

(*b*) *Malformations among other Relatives.*—Malformations among other relatives* were recorded at interview with mothers, but for various reasons the information must be accepted with reservations. First, mothers who have given birth to a malformed infant have a special interest in recalling other examples in their families; second, the person interviewed probably knows more about her own than about her husband's relatives; and third, it was not possible to confirm the type of malformation from central records (as in the case of lethal malformations in the same fraternities). Table XIII shows that eighty malformations of all types were recorded among relatives in 742 families in the malformation group, compared with 28 in 742 families of controls; of these defects, 37 and ten respectively involved the nervous system. The incidence among relatives is higher for anencephalus and spina bifida than for hydrocephalus (Table XIV, opposite).

* Other relatives here exclude sibs; they include parents, grandparents and great-grandparents of the propositus, and all other individuals sharing this common ancestry.

TABLE XIV

PROPORTION OF FRATERNITIES, INCLUDING AT LEAST ONE MALFORMATION, WHICH HAVE MALFORMED RELATIVES

Type of Malformation of Propositus*	No. of Fraternities	Type of Malformation of Relative						Total	
		Involving C.N.S.		Not Involving C.N.S.		Unspecified			
		No.†	%	No.†	%	No.†	%	No.†	%
Anencephalus ..	302	16	5·3	10	3·3	4	1·3	30	9·9
Spina bifida ..	300	14	4·7	13	4·3	3	1·0	30	10·0
Hydrocephalus ..	117	2	1·7	2	1·7	1	0·9	5	4·3
Other malformations	23	1	4·3	1	4·3	0	—	2	8·7
All malformations	742	33	4·4	26	3·5	8	1·1	67	9·0
Controls	742	10	1·4	13	1·8	3	0·4	26	3·5

* Where more than one malformed propositus was recorded in a fraternity, the type of the first born was used for this classification.

† Differences in numbers in Tables XIII and XIV are explained by the few cases in which more than one relative of the same fraternity was malformed.

No doubt the difficulty of recording accurately the number and type of malformations among relatives at risk explains the scarcity of data on incidence. Single instances of recurrence in a family were reported for hydrocephalus (Butler-Smythe, 1889) and spina bifida (Dunn and Salter, 1944; Mills, 1949); but the most interesting data were the result of a large scale inquiry into spina bifida by Hindse-Nielsen (1938). This author noted 0·32 per cent. of affected relatives on the mother's side (fourteen out of 4,367), and 0·15 per cent. of affected relatives on the father's side (eight out of 5,365). Murphy (1940) in an investigation of relatives of malformations of all types also observed that the same defect recurred almost three times as often among the maternal relatives, although the incidence of individuals with a malformation of any type was about equal on the two sides. The difficulty of squaring such an observation with genetic theory led Morison (1945) to question the completeness of the records, and certainly before it is accepted as reliable a much more through examination of the problem is needed.

(*c*) *Consanguinity between Parents of Malformations.*—Three first-cousin marriages (i-iii) and one of second cousins (iv) were noted among parents of the 742 fraternities in the malformation group. Their offspring were as follows.

(i) Four children, all born alive. Three children not affected; one child (the second), with hydrocephalus and congenital cataract, died at 14 days. Father had two children, both normal, by a previous marriage.

(ii) Four children, all born alive. Three children not affected; one child (the fourth), with spina bifida, died at three weeks.

(iii) A single child, stillborn, with spina bifida and hydrocephalus.

(iv) Three children. Two live born, not affected; one stillborn (the second), with hydrocephalus.

For this series the consanguinity rate is 0·54 per cent., and 0·40 per cent. were first-cousin marriages. In the control series of 742 fraternities, there was only

one example of consanguinity (a first-cousin marriage with two children not affected) giving a rate of 0·13 per cent.

Clearly we cannot attach much significance to differences of this order based on records of a few hundred families. In any case we are unlikely to get much help from a study of consanguinity with a condition whose incidence is almost 0·6 per cent. As Hogben (1939) has indicated, where a recessive condition is rare, a high proportion of affected individuals are offspring of near relatives; but where it is common (more frequent than 0·2 per cent.) high rates of consanguinity will not be expected. The literature on malformations contains few reports of the incidence of consanguinity of parents, and none in which the incidence is known for the population from which cases were drawn. Malpas (1937) sent questionnaires to parents of 294 malformations, and recorded no example of consanguinity from 109 replies. Hindse-Nielsen (1938) found three consanguineous marriages among 124 couples who had offspring exhibiting spina bifida, and Murphy reported two first-cousin unions and one of second cousins among 553 couples observed by him. It may be noted that the incidence of first-cousin marriages shown above for parents of malformations and controls is lower than has usually been recorded for the general population. Elderton (1911) gave a figure of 3 per cent.; Hogben (1931) suggested that it varied between 0·5 and 1 per cent., but emphasized the uneven distribution in different sections of the community. There is some evidence (Bell, 1940) that the incidence of consanguinity is falling.

(*d*) *Rhesus Incompatibility*.—It was suggested by Wiener (1946) that at least one variety of spina bifida is produced by Rh sensitization. In support of this view he mentioned three families with erythroblastotic infants which also produced stillbirths with spina bifida, and quoted the experience of L. H. Snyder (unpublished) who observed three Rh-negative mothers (two of them exhibiting Rh antibodies), each of whom produced infants with spina bifida in her first two pregnancies. It is well known that a rhesus incompatibility is rarely present in a first pregnancy, so that the increased predisposition of the first-born to spina bifida (see Part I) could hardly be attributed to this cause. In any case it is not easy to accept the view that a serum incompatibility which affects the nutrition of the embryo in the third week is compatible with its continued development to a viable stage.

Although a number of our cases occurred prior to the discovery of the rhesus factor, or before its importance was generally appreciated, some of the more recent ones were born in hospitals well equipped for haematological investigations which have now become a routine procedure. In no case of spina bifida or other central nervous malformation was the presence of rhesus incompatibility noted. A conclusive answer would require the haematological investigation of an adequate number of malformations and their mothers and of a representative control group. In the absence of more suggestive evidence than is yet available, Wiener's results may reasonably be regarded as a fortuitous coincidence of two conditions neither of which is uncommon.

3. Summary

Information obtained by home visits from 742 mothers of 755 malformations of the central nervous system is compared with that obtained from 742 mothers of 757 births not resulting in malformations. The results are as follows:

(1) Reproductive history of the mother.

(*a*) Menstruation. There are no appreciable differences in age at onset, length of cycle, or duration of flow between the mothers in the two groups.

(*b*) Age at marriage. Women who give birth to central nervous malformations are on the average a little older than other women when they marry.

(*c*) Results of other pregnancies. The abortion rate is much higher for sibs of the malformations than for sibs of controls; the stillbirth rate is higher for sibs of two malformations (anencephalus and hydrocephalus, but not spina bifida); infant mortality rates are not affected. The rate of foetal and infant loss is slightly increased by standardization for parity. The conception immediately prior to the malformation experiences a greater loss than the others, because of higher rates of infant mortality and abortion.

(*d*) Lactation. There is no significant difference in the proportions breast-fed between sibs preceding malformed births and sibs preceding control births.

(*e*) Fertility. There is little in the data to suggest that women who give birth to malformations are less fertile than other women, or that malformations arise when births succeed each other too rapidly. There is some evidence, especially in the case of hydrocephalus, that women are slightly less fertile in the period preceding the birth of a malformation than in that preceding their other conceptions.

(2) Familial incidence of malformations of the central nervous system.

(*a*) The incidence of malformations of the central nervous system in all notified births (live born and stillborn) is 0·59 per cent. The incidence in *all* sibs of a malformed propositus is 1·89 per cent. and that in sibs born *after* a malformed propositus is 5·18 per cent. Thus the risk for any birth following the malformation is almost nine times as great as the average risk.

(*b*) The risk of another malformation is relatively greatest when the first is spina bifida.

(*c*) In each of the three main central nervous malformations, the risk of recurrence of the same malformation is greater than the risk of a different one, but the risk of a different one is greater than that to which the general population of mothers is exposed.

(*d*) Other major malformations not involving the nervous system are not more common among sibs of malformations than among sibs of controls.

(*e*) Malformations, and particularly those of the nervous system, are more common among other relatives (sibs excluded) of fraternities which include central nervous malformations.

(*f*) There were three first-cousin marriages and one of second cousins among parents of 742 fraternities of malformations; there was one first-cousin marriage among parents of 742 fraternities of controls. The investigation of consanguinity for a condition as common as a central nervous malformation is in any case unlikely to be fruitful.

(*g*) No case of rhesus incompatibility was recorded, but many of the births occurred in years prior to the use of the requisite investigation. There are, however, grounds for doubting the aetiological importance of this factor.

Many people assisted the work of this inquiry, and we acknowledge particularly our indebtedness to the following: Dr. Jean Mackintosh, and those members of the Birmingham Maternity and Child Welfare Department who co-operated fully in making available to us the records of the department; Dr. Dorothy Tidmas, who completed a preliminary survey of the malformations of one year; Mrs. K. Gibson, Miss M. Edge, Mrs. Burgess Smith, Mrs. Leaver, Miss Day, Miss Bayes, and certain members of the almoner's department of the United Birmingham Hospitals, all of whom took part in the field work; and Miss C. Wall, who prepared the illustration used in the text. Dr. Enid Charles and Sir Leonard Parsons read the typescript and offered useful suggestions. Finally, and in particular, we record our gratitude to Prof. Lancelot Hogben, F.R.S., who has contributed most generously to this inquiry.

References

Bell, J. (1940). *Ann. Eugen. Camb.*, **10,** 370.
Boyd, J. D. (1942). Clinical Suppl. to *London Hosp. Gazette*, **45,** No. 3.
Butler-Smythe, A. C. (1889). *Lancet*, **1,** 272.
Dunn, H. G., and Salter, J. G. (1944). *J. Obstet. Gynaec. Brit. Emp.*, **51,** 529.
Elderton, E. M. (1911). Eugenics Laboratory Lecture Ser. IV, London.
Hindse-Nielsen, S. (1938). *Acta chir. scand.*, **80,** 525.
Hogben, L. (1931). " Genetic Principles ", Williams & Norgate Ltd., London.
——— (1939). " Nature and Nurture ", George Allen & Unwin, London.
Macklin, M. T. (1936). *Amer. J. Obstet. Gynec.*, **32,** 258.
Malpas, P. (1937). *J. Obstet. Gynaec. Brit. Emp.*, **44,** 434.
Mills, W. G. (1949). *Brit. med. J.*, **1,** 139.
Morison, J. E. (1945). *Ulster med. J.*, **14,** 1.
Murphy, D. P. (1940). " Congenital Malformations ", University of Pennsylvania Press, Philadelphia; (1947). 2nd ed., J. B. Lippincott Co., Philadelphia.
Penrose, L. S. (1939). *J. ment. Sci.*, **85,** 1141.
——— (1946). *Ann. Eugen. Camb.*, **13,** 73.
Pybus, F. C. (1921). *Lancet*, **2,** 599.
Quigley, J. K. (1943). *Amer. J. Obstet. Gynec.*, **46,** 879.
Record, R. G., and McKeown, T. (1949). *British Journal of Social Medicine*, **3,** 183.
Snell, G. D., and Picken, D. J. (1935). *J. Genetics*, **31,** 213.
Still, G. F. (1927). *Lancet*, **2,** 853.
Wiener, A. S. (1946). *Amer. J. clin. Path.*, **16,** 319.

APPENDIX A

DETAILS OF FRATERNITIES CONTAINING TWO OR MORE MALFORMED OFFSPRING

Group I.—Fraternities in which all Malformations are Propositi of the present Series.

Fraternity	Birth Rank	Date of Birth	Result
a	1	1941	Miscarriage
	2*	Oct., '43	Stillbirth—spina bifida, hydrocephalus, and talipes
	3*	March, '45	Death at 13 days—spina bifida
b	1	Jan., '31	Live birth
	2	1932	Miscarriage
	3	Aug., '33	Live birth
	4	?	Miscarriage
	5	?	Miscarriage
	6*	July, '42	Stillbirth—spina bifida
	7*	Sept., '43	Death at 5 weeks—spina bifida
	8	?	Miscarriage
	9	April, '47	Live birth
c	1	Oct., '31	Live birth
	2	Dec., '35	Stillbirth—cause not known
	3	Feb., '38	Live birth. Died at 2 years—broncho-pneumonia
	4*	July, '41	Stillbirth—anencephalus
	5	?	Miscarriage
	6*	Nov., '43	Stillbirth—anencephalus
d	1	July, '40	Live birth
	2*	Sept., '41	Stillbirth—anencephalus
	3*	Oct., '42	Death at 8 hours—spina bifida and hydrocephalus
	4	June, '44	Live birth
	5	July, '48	Live birth
e	1	May, '36	Live birth
	2	Sept., '42	Miscarriage
	3*	Feb., '43	Stillbirth—anencephalus and spina bifida
	4*	Aug., '44	Death at 1 day—spina bifida, hydrocephalus, and talipes
	5	July, '47	Live birth
f	1*	Jan., '41	Death at 7 days—spina bifida
	2	Nov., '46	Live birth
	3*	Sept., '47	Stillbirth—spina bifida and encephalocele
g	1*	July, '45	Death at 6 months—hydrocephalus
	2*	Aug., '47	Death at 14 days—spina bifida
h	1*	Aug., '40	Death at 18 days—spina bifida
	2*	Sept., '42	Death at 1 month—spina bifida
i	1	Sept., '39	Live birth
	2*	Nov., '42	Death at 2 months—spina bifida
	3	Dec., '43	Live birth
	4*	Sept., '45	Stillbirth—anencephalus
	5*	March, '47	Death at 4 days—spina bifida and hydrocephalus
j	1	May, '36	Death at 10 hours—cause unknown
	2*	June, '42	Stillbirth—spina bifida and hydrocephalus
	3*	Dec., '43	Stillbirth—anencephalus and central placenta praevia

* Propositi, i.e. central nervous malformations, included in the present series.

Group I.—continued.

Fraternity	Birth Rank	Date of Birth	Result
k	1*	April, '41	Death at 3 months—spina bifida
	2*	April, '42	Death at 10 days—spina bifida
	3	Nov., '44	Live birth
	4	March, '47	Live birth
	5	Feb., '48	Miscarriage
l	1	Feb., '42	Miscarriage
	2	June, '43	Live birth
	3*	Dec., '47	Death at 1 day—hydrocephalus
	3*		Death at 1 day—hydrocephalus

Group II.—Fraternities in which only one Malformation is a Propositus of the present Series but which also contain an Individual with a Lethal Central Nervous Malformation.

a	1	March, '33	Stillbirth—placenta praevia
	2†	Feb., '34	Stillbirth—spina bifida
	3	March, '35	Live birth
	4	May, '36	Live birth
	5	Oct., '39	Live birth
	6	Oct., '40	Live birth
	7*	April, '42	Stillbirth—anencephalus
	8	Nov., '43	Live birth
b	1†	March, '41	Death at 5½ months—developmental defect of brain and malformation of lungs
	2*	June, '43	Death at 9 months—developmental defect of brain
	3	Oct., '45	Death at 4 months—cause unknown
	4	1946	Miscarriage
c	1†	Sept., '40	Stillbirth—anencephalus
	2	Feb., '42	Miscarriage
	3	June, '43	Miscarriage
	4	Aug., '44	Live birth
	5*	Dec., '47	Stillbirth—anencephalus
d	1†	June, '34	Death at 8 days—spina bifida
	2	Dec., '35	Live birth
	3	Aug., '38	Live birth
	4*	May, '43	Death at 9 weeks—spina bifida and hydrocephalus
e	1†	April, '35	Stillbirth—spina bifida
	2	May, '36	Live birth
	3	July, '38	Live birth
	4	1939	Miscarriage—multiple congenital abnormalities
	5	Oct., '41	Live birth
	6*	Aug., '44	Stillbirth—spina bifida and hydrocephalus
f	1	March, '38	Live birth
	2	Feb., '39	Miscarriage
	3	Feb., '43	Live birth
	4†	June, '44	Death at 1 week—spina bifida and deformity of hands
	5*	Sept., '47	Death at 2 days—hydrocephalus and congenital deformity of heart

* Propositi, i.e. central nervous malformations, included in the present series.

† Cases of stillbirth or infant death due to central nervous malformations not included in the present series.

Group II.—continued.

Fraternity	Birth Rank	Date of Birth	Result
g	1	Aug., '30	Live birth
	2	Feb., '32	Live birth
	3	July, '34	Live birth
	4†	July, '37	Death at 9 days—spina bifida
	5	July, '38	Live birth
	6*	Sept., '40	Stillbirth—anencephalus and spina bifida
	7	Aug., '46	Live birth
h	1	June, '31	Live birth
	2	Nov., '33	Live birth
	3†	May, '35	Stillbirth—spina bifida
	4	June, '37	Live birth
	5	Sept., '38	Live birth
	6	Nov., '40	Stillbirth—cause unknown
	7	Feb., '42	Live birth
	8	April, '43	Death at 6 days—accidental suffocation
	9*	April, '44	Stillbirth—anencephalus
	10	July, '45	Live birth
	11	April, '47	Live birth
i	1†	Feb., '31	Death at 5 days—spina bifida
	2	May, '32	Live birth
	3	Dec., '33	Live birth
	4*	Feb., '40	Stillbirth—anencephalus
j	1	Aug., '36	Live birth
	2	Nov., '38	Live birth
	2†		Stillbirth—hydrocephalus
	3	July, '41	Live birth
	3*		Stillbirth—hydrocephalus
	4	Oct., '44	Live birth
k	1	Jan., '30	Death at 1 month—cause unknown
	2	March, '31	Live birth
	3	May, '33	Live birth
	4	Feb., '37	Live birth
	5†	April, '39	Stillbirth—spina bifida
	6	Oct., '40	Live birth
	7	Jan., '42	Live birth
	8*	Sept., '43	Death at 1 week—spina bifida
	9	Feb., '45	Live birth
	10	May, '47	Live birth
l	1†	Jan., '38	Stillbirth—hydrocephalus
	2*	Nov., '40	Stillbirth—anencephalus
m	1†	May, '37	Death at 3 weeks—spina bifida
	2	Dec., '38	Miscarriage
	3*	March, '40	Stillbirth—anencephalus
	4	July, '43	Live birth
	5	Feb., '45	Live birth
n	1	Dec., '35	Live birth
	2	April, '40	Death at 2 months—pneumonia
	3	Oct., '41	Live birth
	4*	Sept., '43	Stillbirth—anencephalus
	5†	July, '46	Stillbirth—anencephalus

* Propositi, i.e. central nervous malformations, included in the present series.

† Cases of stillbirth or infant death due to central nervous malformations not included in the present series.

Group II.—continued.

Fraternity	Birth Rank	Date of Birth	Result
o	1†	Nov., '39	Stillbirth—spina bifida and hydrocephalus
	2*	April, '46	Stillbirth—spina bifida and hydrocephalus
	3	Nov., '47	Live birth
p	1†	Aug., '38	Stillbirth—anencephalus
	2*	March, '44	Stillbirth—hydrocephalus

Group III.—Fraternities in which only one Malformation is a Propositus of the present Series, but which also contain an Individual with either a Non-lethal Central Nervous Malformation or a Malformation of another System.

a	1*	June, '43	Stillbirth—anencephalus
	2	1944	Live birth—mild degree of spina bifida successfully treated by surgery
	3	1947	Live birth
b	1	Sept., '19	Live birth
	2	Dec., '20	Live birth
	3	May, '23	Live birth
	4	July, '35	Live birth—talipes. Still alive
	5	Nov., '39	Stillbirth—cause unknown
	6*	Nov., '42	Stillbirth—anencephalus
c	1	Sept., '44	Live birth—pyloric stenosis successfully treated
	2*	Dec., '45	Stillbirth—hydrocephalus
d	1	Sept., '42	Live birth
	2*	Jan., '45	Death at 7 days—spina bifida
	3	Aug., '46	Live birth—hydrocephalus. Still alive 2 years later
e	1	Oct., '33	Live birth
	2	Feb., '35	Live birth
	3	July, '37	Live birth
	4	Dec., '38	Live birth
	5	Oct., '39	Stillbirth—cause unknown; imperforate anus present
	6	March, '41	Live birth
	7	March, '42	Live birth
	8	June, '44	Live birth
	9*	Feb., '46	Death at 1 hour—spina bifida
f	1	Nov., '42	Live birth
	2*	Oct., '44	Death at 14 days—occipital meningocele
	3	Feb., '47	Death at 19 hours—congenital defect of heart

* Propositi, i.e. central nervous malformations, included in the present series.

† Cases of stillbirth or infant death due to central nervous malformations not included in the present series.

APPENDIX B

DETAILS OF FRATERNITIES IN THE CONTROL GROUP CONTAINING MALFORMED OFFSPRING

Fraternity	Birth Rank	Date of Birth	Result
a	1	Dec., '32	Death at 1½ years—cerebral tumour
	2	Jan., '34	Live birth
	3	Aug., '39	Live birth
	4*	Aug., '43	Live birth—webbed fingers
	5	April, '47	Live birth
b	1	May, '42	Live birth
	2*	May, '46	Live birth—congenital cataract (familial)
c	1*	Feb., '43	Live birth
	2	April, '44	Miscarriage
	3	Oct., '44	Miscarriage
	4	Sept., '45	Live birth
	5‡	May, '47	Stillbirth—monster, hydrops foetalis
d	1*	Jan., '47	Live birth
	2†	March, '48	Live birth—pyloric stenosis successfully treated
e	1‡	Sept., '41	Stillbirth—gross deformities
	2*	April, '43	Live birth
f	1	Oct., '37	Live birth
	2*	May, '40	Live birth
	3	June, '42	Live birth
	4‡	July, '44	Death at 3½ months—gastro-enteritis following surgical treatment of hare-lip
g	1‡	Dec., '40	Death at 12 days—spina bifida
	2	April, '44	Live birth
	3*	Dec., '47	Live birth
h	1†	Feb., '32	Live birth—imperforate anus successfully treated
	2	Aug., '37	Live birth
	3*	Jan., '40	Live birth
	4	April, '44	Live birth
i	1‡	Jan., '41	Death at 18 days—congenital cardiac defect
	2	Feb., '43	Live birth
	3*	July, '44	Live birth
	4	June, '47	Miscarriage
j	1	Nov., '35	Live birth
	2‡	Feb., '39	Death at 2 months—spina bifida
	3*	June, '41	Live birth
	4	Dec., '45	Live birth
k	1‡	Oct., '39	Stillbirth—cerebral deformity
	2	April, '42	Live birth
	3*	July, '46	Live birth
l	1	Sept., '40	Live birth
	2‡	March, '44	Stillbirth—anencephalus
	3*	Oct., '47	Live birth

* Propositi.
† Non-lethal malformations occurring among sibs of propositi.
‡ Lethal malformations occurring among sibs of propositi.

Control Group.—continued.

Fraternity	Birth Rank	Date of Birth	Result
m	1	Oct., '30	Live birth
	2	Oct., '34	Live birth
	3†	Dec., '38	Live birth—webbed toes of both feet
	4*	Aug., '47	Live birth
n	1	Jan., '29	Live birth
	2	Jan., '32	Stillbirth—asphyxia
	3†	Feb., '34	Live birth—webbed toes of left foot
	4*	Oct., '43	Live birth
	5	July, '45	Live birth
o	1‡	Dec., '36	Death at 4 days—tracheo-oesophageal fistula
	2	Aug., '42	Miscarriage
	3	Aug., '44	Live birth
	4*	March, '46	Live birth
p	1‡	April, '37	Death at 5 weeks—pyloric stenosis
	2	Jan., '41	Live birth
	3	Dec., '46	Live birth
	4*	Dec., '47	Live birth
	4*		Death at 7 weeks—cause unknown
q	1‡	Nov., '33	Death at 2 days—malformation (unspecified type)
	2	Nov., '34	Miscarriage
	3	June, '36	Live birth
	4	Feb., '38	Live birth
	5	July, '39	Death at 4 months—gastro-enteritis
	6*	Feb., '44	Live birth
	7	Jan., '47	Live birth

* Propositi.
† Non-lethal malformations occurring among sibs of propositi.
‡ Lethal malformations occurring among sibs of propositi.

ABSTRACTS

(This section of the JOURNAL *is devoted to selected abstracts of articles on social medicine appearing in the current literature. The section will be edited in collaboration with the two abstracting Journals,* Abstracts of World Medicine, *and* Abstracts of Surgery, Obstetrics and Gynaecology.)

The Effect of Specific Therapy on the Common Contagious Diseases. COOKE, J. V. (1949). *J. Pediat.*, **35,** 275.

The effect of specific therapy on common contagious diseases was assessed by a study of the mortality figures from vital statistics of the U.S. Bureau of the Census, and the morbidity rates tabulated by the U.S. Public Health Service. Since the introduction of the sulphonamide drugs there has been a striking fall in the mortality rates. As penicillin was not generally available until 1945 its effect is not under review.

Death rates from pneumonia are of interest, for the figures for 1945 were half those of 1935, yet when the mortality rates for the different age-groups are scrutinized the fall is seen to be unequally distributed. Thus in 1938, 65 per cent. or less of the deaths occurred in children under one year old, but in 1945 this proportion had risen to 75 per cent. A similar state of affairs occurred in measles and whooping-cough.

At the beginning of the century the mortality rate for diphtheria was 20 per 10,000 and by 1940 it had fallen to 1 per 100,000. This decline can be attributed almost entirely to specific prophylactic vaccination. There has been little tendency for either the morbidity or the mortality rate to fall further since 1940, and, as there are in the U.S.A. almost 15,000 cases annually with over 1,000 deaths, the situation cannot be viewed complacently.

Since 1926 the morbidity rate for scarlet fever has fallen, but not at the same speed as the decline in mortality rate since the advent of sulphonamides.

There has been a dramatic fall in the mortality rate for erysipelas with use of sulphonamides. The morbidity rate has also fallen. According to the author this is due to the fact that the most common type of erysipelas is caused by spread of streptococcal infection from the upper respiratory tract to the skin. Since diseases of the respiratory tract are now treated with sulphonamides this secondary spread of infection is prevented.

Whooping-cough in 1925 displaced diphtheria as the chief cause of death amongst the common infectious diseases; 95 per cent. of these deaths are in children under 5 years. Since active pertussis immunization was started there has been a steady decline in incidence, with a relative increase in deaths amongst infants of under one year. The author suggests that few children under 1 year have been protected, hence a greater proportion of these are attacked, and since it is difficult to administer sulphonamides to them the death rate is higher. This mortality can be combated by immunization during the first year, and use of penicillin in place of sulphonamides.

The cause of death in measles being secondary pneumonia, sulphonamides have caused a reduction in mortality rate, with a relative increase in the rate for children under one year. With the increased employment of penicillin the infantile death rate should diminish.

Although sulphonamides have reduced the mortality rate in meningococcal meningitis, two factors prevent still better results: late diagnosis, and difficulty in drug administration. Increased admission to hospital with increased use of diagnostic lumbar puncture, together with penicillin therapy, should improve future mortality figures.

A. Michael Critchley

Incidence of Infections in Infants in Two Maternity Units. ROSCOE, J. D. (1949). *Brit. med. J.*, **2,** 1144.

All infections occurring in the newborn in two maternity units in Cambridge from May, 1947, to April, 1948, were recorded. Unit A, the larger, accommodated 56 normal cases in four wards. Unit B had ten beds in two wards for cases of abnormal labour. The term infection included any evidence, however trivial, such as the presence of a single pustule, or a " sticky " eye persisting for over 24 hours.

In Unit A the infection rate was 8·3 per cent. (104 cases in 1,257 live births). In Unit B the rate was 10·3 per cent. (nineteen in 185 live births). In A, 68 out of 104 infections involved the eye; in B, there were three out of nineteen, the lower rate being possibly due to protection of the eyes in B with a single layer of gauze during cleaning of the nursery. The infections included rhinitis, enteritis, thrush, pneumonia, otitis media, and chickenpox. Incidence was fairly even throughout the year except for one small epidemic (nine cases of eye and skin infection) in A in March, 1948. There was no death in A due to infection, but in B a premature infant died of otitis media.

Staffing, accommodation, and nursery technique are described, including certain conditions " less than ideal ", these being: (1) restriction of floor space in some nurseries, especially the only nursery of B; (2) no proper provision for isolation; (3) no milk kitchen; (4) no special nursery nurses in A; (5) careless wearing of masks. The reasonably low infection rates are attributed to a low rate of infection in mothers and staff [no maternal morbidity figure is given], and adequate staffing, cross-infections being prevented by barrier nursing and treatment.

Reports of an infection incidence of 20 to 30 per cent. in large nurseries (with up to fifty infants) are contrasted

with the recent low figure of 2·77 per cent. achieved at the Belfast Maternity Home, where the units are small (five to six cots) and frequent thorough cleaning between intakes is possible. It is suggested that by similarly reducing the numbers in unit and nursery, and protecting the infants' eyes from dust, the incidence of infection may be lessened and with that the neonatal death rate.

V. Reade

The Source of Infection in Pemphigus Neonatorum. PARKER, M. T., and KENNEDY, J. (1949). *J. Hyg., Camb.*, **47,** 213.

An outbreak of pemphigus occurred in a twenty-bedded maternity unit, lasting from mid-March to early August. The nursery was overcrowded, containing from fifteen to 25 babies. By transferring about one-third of the mothers and infants to a separate annexe on the 2nd or 3rd day of the puerperium, and discharging infants on the 8th or 9th day, the numbers were kept down with a high turnover. Conjunctivitis was endemic, and diarrhoea began coincidentally with the pemphigus epidemic but continued for some time after the epidemic subsided. *Staphylococcus aureus* was isolated in nineteen out of 36 cases of conjunctivitis but was found in as many stools from healthy infants as from those with diarrhoea.

Nasal swabs were taken from the staff and the mothers at regular intervals; nasal swabs were also taken from all babies as well as swabs from the bullae. For a 5½-week period, daily nasal swabs were taken from the infants. Phage typing was carried out by the method of Wilson and Atkinson (*Lancet*, 1945, **1,** 647).

Staph. aureus was found in all bullae, being of the same type (3A+) in the last nine cases. Three of the strains from eye swabs were typed; two belonged to the same type. Of 613 nasal swabs taken from infants 96 from newborn infants were nearly all sterile. *Staph. aureus* was present in 210 (34 per cent.) and was isolated from about 50 per cent. of cases at the end of the first week. Type 3A+ occurred in 38 infants out of the 54 with *Staph. aureus* in the nose. Phage typing was carried out on less than half of the cultures. A table shows that one type was always predominant, being present throughout the epidemic. The strain was presumably brought into the nursery by some adult, and was carried from child to child. Overcrowding and lack of staff made it impossible to carry out barrier nursing. The possibility of putting the children's cots at the foot of the mothers' beds will have to be considered.

The incidence of nasal infections in the staff was considerably reduced by regular spraying with penicillin. The 3A+ type was last found in a nasal swab from a nurse 1 month before the end of the outbreak.

[The article shows clearly the dangers of large understaffed nurseries and provides further evidence for the wisdom of keeping the baby with the mother, for in no case did the " epidemic " staphylococcal strain appear in a maternal swab.] *J. G. Jamieson*

Stages in the Development of Collective Immunity in Malaria. SWELLENGREBEL, N. H. (1949). *Docum. neer. indon. Morb. trop.*, **1,** 165.

The term " collective immunity " refers to the immunity that develops in a population exposed almost continuously throughout life to malarial infection. It is assumed that the average spleen and parasite rates observed in age groups taken together represent the average course of development of immunity in the people during their lifetime. The strength of immunity, as indicated by these rates and by observations on the crescents and the relative incidence of the species of malarial parasites, varies in different places, and these may be arranged to form an ascending scale of stages in the development of collective immunity.

Schüffner, Swellengrebel, Annecke, and de Meillon (*Zbl. Bakt.*, 1. *Abt. Orig.*, 1932, **125,** 1) concluded, from a comparison of signs of immunity in populations of Sumatra and Java with those found in African negro populations, that the differences observed were racial. N. H. and J. M. H. Swellengrebel (*Ned. Tijdschr. Geneesk.*, 1948, **92,** 3498), however, found parasite rates in Papuans living in highly endemic parts of North-Western New Guinea similar to those in South African Bantu tribes and African negroes in Surinam, Dutch Guiana; they concluded that the opinion of Wilson and Wilson (*Trans. R. Soc. trop. Med. Hyg.*, 1937, **30,** 431) that these differences between Indonesians and Africans were not racial but due to external circumstances had much in its favour.

In the present paper the author reviews the observations made in Indonesia, South Africa, and Surinam and compares them with those of the Wilsons in East Africa and India. He concludes that there is no reason why Western Indonesians, if sufficiently exposed to infection, should not reach the highest stage of collective immunity seen in some groups of Papuans, nor why Papuans should not reach the highest African stage. At present, however, this is not the case so far as is known, and the view of Schüffner *et al.* that the ability to reach the highest stage is a hereditary character has still to be disproved. In Surinam a deterioration within 4 months from a fully immune status raised doubts as to the stability of collective immunity in malaria. The effect of exposure to foreign strains of parasites is touched upon in the case of adults of Surinam.

[The original papers referred to by the author should be read by those interested in this complex subject.]

J. F. Corson

The Nation-wide Campaign against Malaria in Venezuela. GABALDON, A. (1949). *Trans. R. Soc. trop. Med. Hyg.*, **43,** 113.

Venezuela has a population of about 4,000,000 living in an area of 912,000 sq. kilometres. The coastal sector, of less than one-fifth of this area, contains three-quarters of the population and is less malarious than the central area, where about one-fifth of the population lives. Malaria is listed as one of the five major causes of death. In 1936 a special anti-malarial service was inaugurated and survey and drainage work carried out, but conditions did not improve in the rural areas till the advent of DDT. The chief vectors are *Anopheles darlingi*, mainly anthropophilic with a mean sporozoite index of 0·9 per cent., and *A. albimanus*, mainly zoophilic with an index of 0·6 per cent. *Plasmodium falciparum* is the predominant parasite, though below the age of 5 years *P. vivax* is more prevalent. Seasonal periodicity corresponds to rainfall, with slight variations according to the parasite concerned, but a 5-year cycle has been noted.

In 1945 DDT house spraying was started with a 50 per cent. wettable powder made into a 5 per cent. suspension and delivered in the strength of 2 g. DDT per sq. metre. By the end of 1948 the percentage of houses protected by DDT was 37·2 and the malaria death rate had fallen from an average of 112·2 in the period 1941-45 to 14·8 in 1948. These results suggest the possibility of eradicating malaria from the country, but this will depend on the conviction of malariologists themselves that it can be done. *Clement Chesterman*

Phlebotomus and Residual DDT in Greece and Italy. HERTIG, M. (1949). *Amer. J. trop. Med.*, **29**, 773.

It is generally accepted that residual spraying with DDT for the control of the anopheline population automatically results in a reduction of the sandfly population. In the past, in regions where the two insects co-exist, exact data concerning the results achieved have, unfortunately, been confined to the results of anopheline surveys and claims to have reduced the sandfly density rest mainly on general impressions, which are notoriously unreliable. This state of affairs is well illustrated in Greece and Crete, where malaria and leishmaniasis are both prevalent and where an extensive anti-malaria campaign has been in progress for several years, no fewer than 700,000 houses being sprayed with DDT in Greece in 1946. But whereas each year much valuable information has become available concerning the reduction in anophelines and in malaria, in the case of the sandfly the reduction has only been indicated by such phrases as " incidence greatly reduced " or, as was often the case, " sandflies have practically disappeared ".

During 1948, the author and his colleagues, working under the auspices of the World Health Organization-Interim Commission, endeavoured to obtain more exact records than had previously existed concerning the effects of DDT residual spraying on the density of *Phlebotomus* spp., and on the incidence of *Leishmania tropica* and *L. donovani*. Their observations were carried out in Athens and its surrounding villages, in Crete, and also during a short visit to Sicily and Sardinia. The interpretation of the observations recorded concerning *Phlebotomus* density was complicated by various factors. Where " official " sprayings had been carried out there were no exact records of the previous abundance, or otherwise, of sandflies, while in many of the more heavily infested areas not so treated the local inhabitants had purchased and used insecticides on quite a large scale. Moreover, observations on the incidence of leishmaniasis amongst the human population had to be considered in relation to fluctuations in the canine reservoir of the disease. Thus in Canea, in Crete, there had been a very marked decline in the incidence of kala azar, but this was shown to have occurred before the use of DDT and was probably the result of the selective destruction of infected dogs and of a general reduction of the canine population. It is of great interest to compare this fall in the incidence of *L. donovani* infection following the reduction of the canine reservoir, with an equally notable drop in the incidence of *L. tropica* infection observed in certain villages in Crete, which was unquestionably associated with the reduction in sandflies resulting from the use of DDT for malaria control.

In view of the many potential factors which might influence his deductions, the author refrains from drawing any sweeping conclusions from his extensive observations, the results of which are carefully analysed; nevertheless, he considers that " the following general conclusions seem warranted: (*a*) Treatment of interiors with residual DDT gives immediate and virtually complete protection from sandflies indoors. (*b*) House spraying alone, in compact communities, with an annual, preferably pre-season, treatment, eventually reduces the *Phlebotomus* population within the sprayed areas to near the vanishing point."
R. M. Gordon

Planning the Control of Sleeping Sickness. MORRIS, K. R. S. (1949). *Trans. R. Soc. trop. Med. Hyg.*, **43**, 165.

The author claims that in a limited area to the east of the Volta river, Gold Coast, the incidence of human trypanosomiasis has been reduced by 97·5 per cent. in the ten years 1938-47. The method used is termed " selective clearing " and consists in removing, along a complete river system, only those forms of vegetation which are an essential constituent of the dry-season habitat of the tsetse. The tsetse communities of *Glossina palpalis* and *G. tachinoides* disappeared when clearing was completed and the cleared areas were readily farmed by the people, a population density of 20 to the sq. mile (7·7 to the sq. km.) being sufficient to maintain clearance. In addition, selected sites such as ferry or ford crossings and washing and drinking water sites were cleared. Attention to the tributaries along which the people lived was more important than attempting the too costly task of clearing the main river banks. The author considers that this method is cheaper and more effective than the so-called " protective clearing " of wide areas round human habitations, and more radical than chemotherapeutic measures, with regular mass surveys and treatment centres. [The method seems well adapted to this area, where a dry season drives the flies to seek cover in restricted areas, but it is doubtful if it could be applied to the rain forest regions, where there is little or no seasonal variation.] *Clement Chesterman*

Mass Penicillin Prophylaxis. An Experiment with Negative Results. KUH, C., and COLLEN, M. F. (1949). *J. Amer. med. Ass.*, **140**, 1324.

This experiment was designed to test the value of orally administered penicillin as a prophylactic measure against intercurrent infections. The subjects were members of a voluntary health insurance plan and included all age groups above 7 years; they were divided by random sampling into a group of 1,486 persons receiving penicillin tablets and a control group of 1,451 receiving tablets of calcium carbonate of similar size. During the course of a year there was a gradual diminution in the numbers continuing to attend, and during the last month only 631 persons were still participating in the experiment—295 in the penicillin group and 336 controls. All persons were asked to submit a monthly report, giving details of illnesses, time lost from work or other activities, visits to doctors, and treatment in hospital: 9,264 such reports were received—4,582 from persons taking penicillin and

4,682 from controls. At the start of the experiment the dose of penicillin was 50,000 units twice daily; after 4 months the dose was increased to 100,000 units twice daily, and after a further 3 months it was again increased to 200,000 units twice daily. The numbers of monthly reports during these three periods were 3,582, 3,685, and 1,997 respectively.

Analysis of the reports showed that oral penicillin in the dosage used had no prophylactic value. There were no significant differences between the treated and control groups as regards incidence of respiratory or non-respiratory disease, time lost from work, frequency of visits to doctors, and admissions to hospital, or between the results in the different age groups. Nevertheless many patients reported subjective benefit both from penicillin and from the control tablets. Mild toxic reactions were reported by ninety patients receiving penicillin and by 64 patients receiving control tablets, the commonest complaints in both groups being indigestion, skin lesions, and headache. *A. R. Kelsall*

The Inheritance of Sickle Cell Anemia. NEEL, J. V. (1949). *Science*, **110**, 64.

The blood of both parents of thirteen persons suffering from sickle-cell anaemia, and of one of the parents of sixteen others, was examined for sickling. All these parents showed the sickle-cell trait. This strongly supports the hypothesis that a dominant gene is responsible, which in heterozygotes gives rise to sickling, and in homozygotes to sickle-cell anaemia. A small proportion of heterozygotes may also develop anaemia.

J. A. Fraser Roberts

The Genetics of the Sickle-cell Trait in a Bantu Tribe. BEET, E. A. (1949). *Ann. Eugen., Camb.*, **14**, 279.

Of 308 children, aged 6 to 18 years, of a pure-stock Bantu tribe, the sickle-cell trait was found to be present in 13·6 per cent. Family studies showed that the trait behaves as a Mendelian dominant. It is suggested that sickle-cell anaemia occurs in the homozygotes only.

J. A. Fraser Roberts

The Incidence of Parental Consanguinity in Diabetes Mellitus. HARRIS, H. (1949). *Ann. Eugen., Camb.*, **14**, 293.

The incidence of consanguineous marriages amongst the parents of a series of diabetics was found to be higher than the normal. This, however, was confined to those developing the disease relatively early in life. In 505 subjects whose age at the time of onset was under 30 there were ten instances of parental consanguinity of all degrees compared with an expectation of 3·6. The difference is significant. On the other hand, amongst those over 30 at the time of onset the observed and expected figures were almost identical. It is concluded that there are genetical differences between diabetes of early and of late onset and that the former may be determined by one or more recessive genes.

J. A. Fraser Roberts

Hereditary Factors in Infantile Progressive Muscular Atrophy. Study of One Hundred and Twelve Cases in Seventy Families. BRANDT, S. (1949). *Amer. J. Dis. Child.*, **78**, 226.

A study of 112 cases of Werdnig-Hoffmann's disease among the siblings of seventy families served to show the extremely complicated genetic factors at work. It would appear that recessive inheritance is a likely cause and the high consanguinity rate (eight times higher than in a control group) favours this theory. However, some families showed incomplete dominance. Variations in the course and severity of the disease were frequent as between families, but most unusual in any given family. This, the author concludes, suggests the existence of two or more co-acting genes. *Wilfrid Gaisford*

The Mandibulo-facial Dysostosis. A New Hereditary Syndrome. FRANCESCHETTI, A., and KLEIN, D. (1949). *Acta ophthal., Kbh.*, **27**, 143.

In this monograph the authors give an excellent and exhaustive illustrated description of the peculiar syndrome first described by Franceschetti in 1944.

After a thorough clinical and genetical analysis of six personal observations, the cases from the current literature are dealt with and the clinical features are discussed. The chief features of mandibulo-facial dysostosis are: (1) palpebral fissures sloping downwards laterally, with a coloboma in the outer portion of the lower lid; (2) hypoplasia of the facial bones, especially the malar bones and the mandible; (3) malformation of the external ear; (4) macrostomia, high palate, and malocclusion of the teeth; (5) blind fistulae between the angles of the mouth and the ears; (6) atypical hair growth.

The patients present so many common features that they look like siblings. There are complete or typical forms, and incomplete, abortive, unilateral and atypical forms. Inheritance is irregularly dominant. The pathogenesis is that of an inhibitory process occurring towards the seventh embryonic week and affecting the facial bones (from the first visceral arch). The authors adhere to the theory of a disturbance of the action of the organization centre probably due to a lethal or sublethal effect of the gene concerned. The relation to other types of cranial dysostosis (such as Crouzon's dysostosis) is mentioned. *E. Godtfredsen*

Genetics of Atherosclerosis. Studies of Families with Xanthoma and Unselected Patients with Coronary Artery Disease Under the Age of Fifty Years. ADLERSBERG, D., PARETS, A. D., and BOAS, E. P. (1949). *J. Amer. med. Ass.*, **141**, 246.

On the basis of a study of a considerable number of families and isolated cases, the authors conclude that the common basis of most cases of coronary atherosclerosis in patients below the age of 50 years may be an inherited disturbance of the cholesterol metabolism which manifests itself in an elevated blood cholesterol level (above 300 mg. per 100 ml. of blood). Familial xanthomatosis is the severest form of this inherited disturbance. Xanthelasma and arcus corneae are other stigmata of the same condition, while hypertension does

not seem to form part of the disease. [The suggestion that the condition is inherited as a semi-dominant character with irregular manifestation appears plausible. On the other hand, the identification of the more severe clinical pictures with homozygotes and the less severe (and subclinical) cases with heterozygotes for the gene in question would require a much firmer genetical basis than that presented by the authors.] *H. Grüneberg*

Hereditary Stenosis of the Aqueduct of Sylvius as a Cause of Congenital Hydrocephalus. BICKERS, D. S., and ADAMS, R. D. (1949). *Brain*, **72**, 246.

The authors describe a case of stenosis of the aqueduct of Sylvius in a hydrocephalic newborn male infant. Two other male children in this family and four of six males in the preceding generation had been born with hydrocephalus. The brain had the characteristic appearance of advanced hydrocephalus due to distension of the lateral ventricles. In the cerebrum the histological changes consisted of destruction of ependyma, subependymal gliosis, foci of microglial phagocytes in some parts of the white matter, and relative preservation of the cortex. The fourth ventricle was normal in size, the foramina of Majendie and Luschka were patent, and the subarachnoid normal in appearance. The marked dilatation of the lateral and third ventricles was due to stenosis of the aqueduct of Sylvius. Though not occluded at any point it showed definite narrowing of its middle portion. Presumably the narrowed aqueduct was functionally incompetent so that cerebrospinal fluid was formed more rapidly than it could escape from the third ventricle. There was nothing to indicate that the aqueduct was crowded by a faulty migration of primitive neuroblasts and spongioblasts, nor was there any astrocytic hyperplasia or other histological evidence of an inflammatory process. Ependymal rosettes, which are believed by some workers to indicate a premature closure of the neural tube, were present, but since these are commonly found in the raphe of the mid-brain, in the lateral recess of the medulla, and near the central canal of the spinal cord in normal cases, their exact significance must remain in doubt.

The pedigree in this case was so short that it was impossible to determine whether the dominance in males was due to the presence of a sex-linked factor or to a difference in penetrance of the affected genes. However, it provides substantial evidence in support of the occurrence of stenosis of the aqueduct of Sylvius as an inherited abnormality. *R. M. Stewart*

Female Sterility and its Treatment. (Die weibliche Sterilität und ihre Behandlung.) SIEGERT, F. (1949). *Zbl. Gynäk.*, **71**, 367.

The author mentions a variety of causes of sterility—psychological, physiological, and pathological—and stresses the need for a careful and complete examination in all cases. Increased knowledge of female sex hormones and the use of tubal patency tests have aided and clarified diagnosis but have not increased perceptibly the number of cases successfully treated.

During the last 10 years the number of women in Freiburg seeking advice increased fourfold. The author analyses certain points in 461 cases seen at his clinic. The majority of patients (75·1 per cent.) were between 26 and 35 years; 14·8 per cent. were between 35 and 45, and only 10 per cent. between 20 and 25 years. The fertility rate begins to fall after the 30th year, more markedly after the 35th year, and. in multiparae, steeply after the 40th year. Advice was sought in 24·3 per cent. of cases of primary sterility within 2 years of marriage, in 45 per cent. after 3 to 6 years, and in 17·6 per cent. between 7 and 10 years after marriage. Siegel believes that after 5 years of married life the chance of a first pregnancy occurring is only 2 per cent., but in this series 11 to 18 per cent. of patients conceived after 6 to 10 years of sterility, while 5 per cent. conceived after 10 years. The duration of treatment necessary was slightly more prolonged when the period of sterility was long—7·6 months when sterility was of 2 years' duration and 12 months when of 8 years' duration.

Investigation of sterility in 461 cases showed that in 165 (35·2 per cent.) the cause was tubal. In 153 cases the diagnosis was made by salpingography. Salpingography was carried out in 266 cases in preference to insufflation (seven cases) as the author considers it more reliable, particularly in cases of unilateral blockage. He believes that salpingography is without danger provided the patient has been examined and found to have no disease of the adnexa, stays in bed for 2 days, and is investigated during the first half of the menstrual cycle, but that there is a slight risk of producing mechanical obstruction by irritation of the tubal and peritoneal epithelium by "lipiodol". Bilateral closure was present in 79 cases and unilateral closure in 59 cases. Laparotomy was carried out in 26 of the 79 cases of bilateral closure and the finding was confirmed in 15 cases only.

The cause of sterility was ovarian in 28·6 per cent., uterine in 19·5 per cent., and constitutional in 18·2 per cent. of the cases. Tubal obstruction is, in the author's view, rarely due to appendicitis; it may be the result of a previous abortion, a history of which was only obtained in 7 per cent. of the cases. Tuberculosis of the tubes accounts for a small number of cases, but in the largest number of cases the cause was not discovered.

Of 267 patients treated and followed up, 65 (23·9 per cent.) became pregnant; 45 had living children.

Gladys Dodds

Contraception among Two Thousand Private Obstetric Patients. GUTTMACHER, A. F., TIETZE, C., and RUBIN, S. (1949). *J. Amer. med. Ass.*, **140**, 1265.

The authors investigated the contraceptive history and practices of 2,000 private obstetric patients living in and around Baltimore. Over 99 per cent. of the patients were white, more than 85 per cent. were aged between 20 and 35, and about 90 per cent. were in the professional and business classes. The following four questions were put to patients at the first antenatal visit, which usually took place at about 8 to 9 weeks of pregnancy: (1) Did you use contraceptives ? (2) What method did you employ ? (3) Was this pregnancy planned ? (4) When was contraception discontinued ?

From these investigations the following facts came to light. Of these patients 65 per cent. had conceived after abandoning contraception in order to become pregnant, while 17 per cent. had never used contraceptive methods

and in 19 per cent. contraceptive measures had failed. Hence it appears that 80 per cent. of these patients had wanted pregnancies; but this does not take account of those who attended the illegal abortionist when contraception failed. The most popular contraceptives were the condom and the diaphragm, which together totalled 85 per cent. of the contraceptives used. These two together proved the most effective.

Of the planned pregnancies 60 per cent. occurred within 3 months and 90 per cent. within one year of the cessation of contraception. This does not, of course, account for the unknown number in whom the cessation of contraception was not followed by pregnancy.

Elaine M. Sunderland

The Process of Gestation and its Effect on Idiopathic Epilepsy. (Gestationsvorgänge und genuine Epilepsie.) HIRSCHMANN, J. (1949). *Dtsch. med. Wschr.*, **74,** 1110.

Of 231 female epileptics admitted in the years 1925 to 1948 to the Kretschmer Clinic, Tübingen, 28 had their first attack during gestation. In 151 cases pregnancy, parturition, and puerperium had no influence upon the frequency of the seizures. In four cases there was temporary and in one permanent improvement; in 23 there was temporary and in seventeen permanent deterioration during gestation. The frequency of attacks were therefore only permanently affected in eighteen cases (7·8 per cent. of the series). The analysis of the group in which deterioration occurred showed that in eleven cases it occurred during pregnancy, in one case during parturition, in one in the puerperium, and in four cases during lactation. As a rule deterioration occurred during the first gestation. The number of pregnancies with no influence upon the attacks decreased with age, but the number of cases observed was too small for any conclusions to be drawn.

A connexion between hormonal factors and manifestations of epilepsy is suggested. In 22 per cent. of cases seizures started with the first menstrual period; they occurred predominately at the time of the period in 17·3 per cent. In 10·8 per cent. menstruation had stopped or become irregular. In 32·2 per cent. there were suggestions of endocrine disturbance. Of the seventeen patients in whom gestation caused deterioration twelve were of dysplastic or aplastic type, pale and fat, with irregular or late periods and disturbances in water metabolism. This constitutional inferiority was in the author's opinion responsible for the deterioration during gestation.

Mental deterioration, observed in five cases after several pregnancies, is regarded as another indication that the frequency of attacks will increase during gestation.

R. Klein

Relation of Birth Weight to Physical Development in Childhood. ILLINGWORTH, R. S., HARVEY, C. C., and SHANYAH GIN (1949). *Lancet*, **2,** 598.

The authors have carried out a statistical survey of the records of 2,426 Sheffield children in order to establish the relation between birth weight and subsequent physical development. Birth weights were obtained from the midwives' antenatal charts and hospital and infant welfare records rather than from the mothers (it having been found that of 110 mothers, 10·4 per cent. were over 8 oz. (250 g.) wrong in their recollection of the birth weight of their children). On this basis, the children were divided into four groups—5½ lb. (2·5 kg.) or less, 7 lb. 2 oz. to 7 lb. 6 oz. (3·2 to 3·3 kg.), 8½ lb. to 9½ lb. (3·8 to 4·3 kg.), and 9½ lb. or more. There were 517, 712, 940, and 257 children in the respective groups, approximately equally divided between boys and girls. Records of height and weight were obtained from the child welfare clinics and school medical officers. Small samples of from four to 36 of each sex in each birth weight group were taken in half-yearly age groups—from 2 to 13 years for weight and from 4½ to 13 years for height. The authors found a constant uniformly graduated difference in weight between those of the lowest and those of the highest birth weight groups; for instance, a difference of 5·3 lb. (2·5 kg.) in boys aged 5 years and of 11·2 lb. (5·1 kg.) in girls aged 7 years. The difference in height was not so marked, but was definite, there being 2 to 6 cm. difference in average height at all ages between the lowest and highest birth weight groups. Similar differences were found in limited samples whose developmental and nutritional status was assessed by means of the Wetzel grid and Tuxford index.

The roles played by body build, maternal malnutrition, and nutrition in infancy are discussed, with special reference to animal experimental work. The importance of these factors in influencing physical development, and the need for their study in future surveys of this kind, are emphasized and it is suggested that the commonly used developmental charts of weight and height may need to be modified so that birth weight may be taken into consideration. It is pointed out that no indication is given in the authors' records of the effects of the onset of puberty.

[It is to be deplored that there is no statement of the statistical validity of the data and conclusions in this paper, which is entirely based on statistics.]

David Morris

The Mentally Subnormal and Social Medicine. BAILEY, R. (1949). *Edinb. med. J.*, **56,** 369.

A review is made of the investigations on problems of mental deficiency which have been carried out since 1906 in Great Britain. The author hopes "that as the National Health Service develops we may be able to deal with these problems more comprehensively than has been possible in the past".

A. Michael Critchley

Cancer of the Tongue. A Review of 330 Cases. GIBBEL, M. I., CROSS, J. H., and ARIEL, I. M. (1949). *Cancer*, **2,** 411.

Of all patients with cancer admitted to the Hines Hospital, Illinois, U.S.A., from 1931 to 1946, 1·8 per cent. had cancer of the tongue. The incidence in coloured patients was similar to that in white. Syphilis appeared to be an aetiological factor, for 22 per cent. had a positive complement-fixation reaction compared with only 5 per cent. among all patients admitted. There did not seem to be an undue prevalence of oral and dental sepsis, although 10 per cent. had leukoplakia; in many this responded well to massive doses of crude brewers'

yeast. A double primary lesion in the tongue was seen only once in the series of 330 patients, but an unrelated primary malignant growth in some other part of the body was found in seven. The more differentiated cancers were commoner in the anterior two-thirds of the tongue, while the anaplastic cancers were commoner at the base. About half of the growths occurred in the latter situation and in 80 per cent. of these the lymph nodes were already affected when they were first seen, compared with 50 per cent. in growths of the anterior two-thirds. The authors comment on the delay in treatment as compared with other series. Distant metastases were rare, being present in only ten of the 72 cases coming to necropsy. They were usually in lungs or liver. Biopsy examination was carried out for all suspicious lesions and repeated if negative.

Treatment was mainly by deep *x* rays, with interstitial radon seeds in many cases in addition. Surgery was sometimes used as well, but rarely as the sole treatment. The 5-year survival rate in cases without cervical metastasis was 43 per cent., but in patients with cervical metastasis it was 4·6 per cent. The over-all 5-year survival rate was 14 per cent., rates being equal for growths of the base and those of the anterior two-thirds. In view of the poor results in patients with cervical metastasis the authors have, in the past 2 years, employed radical surgery when the metastases are unilateral. Their operation consists of block resection of the area of primary growth and the lymph nodes, together with half the mandible. *H. J. Croot*

Statistical Study of Uterine Carcinoma. (Contribucion al estudio estadistico del cáncer de útero.) RECASENS MÉNDEZ-QUEYPO DE LLANO, M., and E. (1949). *Rev. esp. Obstet. Ginec.*, **8,** 378.

A statistical study is presented of cases of cancer of the uterus seen in the gynaecological clinic of the Faculty of Medicine at the University of Seville from May, 1931, to the end of 1947.

Of 922 cases of cancer of the uterus observed, 829 were cases of cancer of the cervix, and 93 cases of cancer of the corpus, a ratio of 8·6 to one. Of the 829 cases of cancer of the cervix, thirteen arose in cervical polypi. Cancers of the cervix were classified as follows: 490 exophytic, 255 endophytic, 31 laminated, and forty infiltrating. There was a family history of cancer in 66 cases and a history of obstetric dystocia in 4·12 per cent. In five cases a polyp of the cervix had been extirpated.

The age of onset was widely spread over the various age groups. The majority of lesions of the cervix were found at ages between 41 and 60, but there was a relatively higher incidence of carcinoma of the corpus in women over 61 years of age. Parity appeared to influence the incidence; more cancers of the cervix and of the corpus occurred in parous women, but the number of children borne appeared to have little relation to incidence, except that the incidence of cancer of the uterus was higher in women who had borne nine or more children.

In treatment, surgery is preferred for cancer of the cervix except in stage III, when radium and *x* ray therapy are used. The operation of Schauta with Schuchard's paravaginal incision is preferred except in cases where extraction of the uterus by the vaginal route is difficult, when Wertheim's hysterectomy is performed. For carcinoma of the corpus the treatment of election is by surgery, though when the condition of the patient is poor or the tumour extensive, radium treatment is given. Vaginal hysterectomy is considered the treatment of choice though, in unsuitable cases, abdominal total hysterectomy is carried out.

Of the cases of cancer of the cervix 21·6 per cent. were operable. Vaginal operation was performed in 158 with an operative mortality of 16·96 per cent., and abdominal operation in fifteen with an operative mortality of 32·25 per cent. These mortality rates are high, but many of the patients were under 36 years old and these operations were performed before the era of sulphonamides. For cancer arising in a polypus, operation was undertaken in six cases with a mortality rate of 16·67 per cent. Treatment with radium was carried out in 55·85 per cent. of cases of cancer of the cervix. In 22·55 per cent. of cases of cancer of the cervix the condition was far advanced and only symptomatic treatment was possible. The operation rate in 93 cases of cancer of the corpus was 52·68 per cent. Vaginal hysterectomy was performed in 37 with a mortality rate of 2·85 per cent. In twelve cases of abdominal hysterectomy there was no mortality. Radium treatment was given in 28 cases of cancer of the corpus, while in sixteen cases only symptomatic treatment was possible. *Josephine Barnes*

Tuberculosis in Nurses. Clinical Observations on its Pathogenesis as seen in a Fifteen Year Follow-up of 745 Nurses. BADGER, T. L., and AYVAZIAN, L. F. (1949). *Amer. Rev. Tuberc.*, **60,** 305.

The main interest of this study lies in the long duration of the follow-up observations. The study was carried out on a group of 745 nurses who had been originally admitted as students to training school at the Boston City Hospital. In this hospital cases of tuberculosis were scattered throughout the medical wards. No nurse was included in the study unless she had been under observation for over 5 or under 15 years.

Of the nurses 362, or 48·6 per cent., were tuberculin negative on entry; in 285 the reaction became positive; of these 38 (13·6 per cent.) developed tuberculosis. On entry 374 were tuberculin positive; 31 of these (8·3 per cent.) developed tuberculosis. Of the forty cases developing in nurses tuberculin negative on entry, two arose after training, 33 (82·5 per cent.) arose in the first 2 years after conversion of the reaction, three (7·5 per cent.) in the next 3 years, three (7·5 per cent.) in the following 5 years, and two (5 per cent.) between 11 and 15 years after conversion of the reaction. Of the 31 cases developing in nurses tuberculin positive on entry, ten (32 per cent.) arose in the first 2 years, twelve (39 per cent.) in the next 3 years, nine (29 per cent.) in the following 5 years, and none subsequently. The authors confirm the finding of many other workers that the pulmonary lesions developing in initially tuberculin-negative and tuberculin-positive persons are clinically and radiologically similar. They conclude that " most, if not all, of the disease in this group was primary, first infection tuberculosis, whether it appeared in the initial reactor or non-reactor to tuberculin ". [The argument leading to this conclusion is obscure.] *M. Daniels*

Tuberculosis in Coloured Races. I. Pathological Observations on Tuberculosis of Indonesians in Batavia in 1946. II. The Types of Tuberculosis in Coloured Races and in Special Circumstances. III. The Rate of Infection and Reinfection in Tuberculosis. [In English.] STRAUB, M. (1949). *Docum. neer. indon. morb. trop.*, **1**, 117, 225, 347.

The first of these three papers treats of pulmonary tuberculosis among Indonesians in Batavia purely from the pathological aspect and almost solely from that of pathological anatomy. It is based on the very slender foundation of the post-mortem examination of 63 Indonesian patients, mostly tramps who had " often travelled from other parts of the country in a last effort to gain a living in the ' metropolis '. Many of them only came to the hospital to die". The author divides cases of primary infection, according to the pathological findings, into three types: (1) Primary tuberculosis of the childhood type with involvement of the lymph nodes. (2) Primary tuberculosis with greatest activity in the lungs—an acinous pneumonia with subsequent caseation and breaking down of the lymph nodes which may end in rupture into a bronchus and a florid phthisis, or into a blood vessel with dissemination and generalized miliary disease. There is no need in such cases to bring in the question of a hypothetical re-infection. (3) In those cases in which, as is more common in adolescent and adult life, there is primary apical infection of a lobe, cavitation occurs earlier, the adenitis will correspond with the focal area, and pleurisy is a fairly common complication. In the author's series, the instances of primary disease constituted by far the majority. Thus, out of 63 cases, there were seven in which the primary complex was limited or healed, in fourteen there were complications, in eleven lesions of the childhood type of primary tuberculosis, and in eighteen primary disease with cavitation; in thirteen only was there clear evidence of re-infection, in four pulmonary, and in nine limited or disseminating. [Neither in the text nor in his bibliography does the author refer to the much more extensive and detailed work on 300 necropsies on tuberculous subjects in China, published as a M.R.C. Special Report, No. 149, in 1940.] *H. Scott.*

The Management of Mass Radiography Suspects. A Two-year Follow-up. ASPIN, J. (1949). *Tubercle, Lond.*, **30**, 170.

This is a most valuable analysis of the gains of random mass miniature radiography (M.M.R.). The author reviewed 526 full-size skiagrams showing post-primary tuberculosis out of about 34,000 Leeds volunteers. Of the smaller group 233 findings were discarded as insignificant, though in 24 of these lesions were extensive (in four of these the condition progressed later); 293 cases referred to the clinic for observation were divided into two groups, those with minimal lesions (232) and those with advanced (44 moderately and seventeen far advanced). Amongst the 526 patients with radiographic changes 441 had minimal lesions, radiologically classified as " calcifying " (50 per cent. of this group), " soft and calcifying " (25 per cent.), and " patchy or mottled " (25 per cent.). Though " the very numerous calcifying lesions must represent the residues of once more extensive soft lesions . . . they have retrogressed without ever having given rise to recognized illness ".

Analysis of 206 cases of " minimal lesions " followed up for 2 to 4 years showed that of 85 purely calcifying lesions only one spread and seven healed, of 55 soft and calcified lesions eleven spread and twelve healed, and of 66 patchy or mottled lesions 21 spread and nineteen healed. The rest remained unchanged. Spread in half the cases occurred within 1 year. Though on radiological grounds groups in which spread is more likely can be selected, no individual forecast can be made. Apart from radiological progression, changing symptoms and signs, toxaemia, and positive sputum led to classification of the subject as a sufferer from tuberculosis in need of treatment. In those suspected on radiological grounds of tuberculosis but with no symptoms, no signs, no history, and no sputum, radiological signs of progression, stability, or regression must decide the issue. Of these suspects 29 were eventually classified as suffering from tuberculosis, fourteen after a period of apparent stability. " However completely suspects are investigated, delayed spread cannot be avoided " unless every suspect is taken off work—an impossible proposition.

Thus, of 34,000 volunteers radiographed within one year, ninety suffering from tuberculosis were discovered. Of these, 51 unsuspected cases with positive sputum and their family contacts were helped most, 31 with negative sputum being also helped to a lesser degree. A rough estimate of the total expenditure (1944-46) " suggests that it costs about two shillings to *x*-ray each volunteer and about £60 to find each sufferer. Present day costs will be appreciably higher." " If one potential sufferer is overlooked more than 300 have been *x*-rayed in vain."

[The abstractor has repeatedly suggested that random miniature radiography of apparently healthy people is wasteful and purposeless, and that the radiographers should concentrate on the suspected and the endangered section of the population. (*Publ. Hlth., Lond.*, 1944, **58**, 7; *Lancet*, 1947, **2**, 955.) See also *Memorandum of the N.A.P.T. Council*, February, 1949.]

E. G. W. Hoffstaedt

Diseases of Malnutrition and their Sequelae in Inmates of Concentration Camps. (Sultsygdommen og dens følgetilstande hos koncentrations lejrfanger.) HELWEG-LARSEN, P., HOFFMEYER, H., KIELER, J., THAYSEN, E. H., THAYSEN, J. H., THYGESEN, P., and WULFF, M. H. (1949). *Ugeskr. Læg.*, **111**, 1217.

This long report, which is described as a preliminary communication, is based upon the examination of 572 survivors of the political prisoners taken by the Germans in Denmark, and of 710 of the Danish policemen deported by the Germans in September, 1944. The authors describe the diet and general conditions in the concentration camps, and report in detail the various symptoms and effects of prolonged starvation: cachexia, oedema, polyuria, diarrhoea, anaemia, muscular atrophy, avitaminoses, glandular changes, and infections. They deal with the mental effects of imprisonment and starvation, and discuss the changes that occur after release and repatriation. The various disorders and diseases cleared up to a varying degree and at varying rates, but the outstanding impression in this survey was the high rate

of tuberculosis among the survivors, diagnosed up to three years after their return. The other feature disclosed by the investigation was the high incidence of neurosis among the survivors. Altogether 286 of the survivors were unfit for work for periods of two months or more after their return. This was due to general weakness in 5 per cent., tuberculosis in 34 per cent., psychological disorder in 42 per cent., and other diseases in 19 per cent. *B. Nordin*

Relation of Nutrition to Infection in Children. RAWLINGS, J. M. (1949). *Amer. J. publ. Hlth*, **39,** 858.

This paper describes a clinical study of 315 children referred to the Mott Foundation Children's Health Centre because of some chronic infection or faulty nutritional condition. The children's ages ranged from 2 to 17 years, the period of observation from 3 to 32 months. In addition to appropriate medical advice and treatment, all patients received a supplement of vitamins A, B, C, and D; a few received iron and liver. [The indications, preparations, and doses are not given.]

Some form of chronic infection was found in 304 children (96·5 per cent.). The commonest condition was disease of the tonsils (72 per cent.) [the diagnostic criteria are not stated]; the next commonest was involvement of the upper anterior cervical lymph nodes. The author found that in this group 96·4 per cent. were improved as regards the infection and the nutritional state, after 3 months of the supplemental therapy. It is also stated that out of 227 children who at the time of the first examination were considered to need removal of tonsils and adenoids, 133 were found at the end of that period of observation to have improved to a point where the operation was not needed [a not uncommon happening whatever treatment is given]. A faulty nutritional status was observed clinically in 39·5 per cent. of the cases. The commonest complaints made by the mothers regarding these children were of poor appetite and nervousness.

After a 10-month observation period and supplementation alone 82·9 per cent. of children were well, very much improved, or much improved; 90 per cent. of children were improved to a similar degree when, in addition to supplementation, tonsils and adenoids were removed. *P. T. Bray*

Dietary Control of Dental Caries. CIOFFARI, M. S. (1949). *Arch. Pediat.*, **66,** 233.

Statistics have shown that dental caries is probably the most widespread disease of Western civilization. The outstanding difference between the diets of primitive and civilized man is the presence in the latter of a great deal of refined sugar. To investigate the possible harmful effect of refined sugar on the teeth the controlled experiment described in this article was carried out.

"Two groups of fifty children each were observed regularly from birth until 5 years of age, as to their dental condition. One group had very few sweets in their diet, with additional emphasis on the coarseness of food, and on regular vitamin supplements. The other, or control group, had the average American diet with plenty of sweets and irregular vitamin supplements; both groups used the same water supply."

It was found that at 5 years of age 78 per cent. of the group under diet control had no visible cavities, the average being 0·18 cavities per child, while the control children had 5·22 cavities per child, and only 6 per cent. had no cavities. These results suggest the following conclusions. "The balance of evidence points to easily fermentable carbohydrates, especially sucrose, as the main offenders. A child's diet, at least until 7 to 8 years of age, should include (*a*) a bare minimum of sweets, (*b*) a good amount of coarse foods, and (*c*) a maintenance amount of vitamins. In addition, it might be advisable to give the unavoidable quota of sweets at the beginning of the meal only, and to have a raw, coarse fruit or vegetable at the end, with raw fruit for snacks." A further conclusion was that tooth brushes and tooth paste are of less value than suitable diet.

[From the facts supplied, the conclusions drawn are reasonable and support the advice usually given in Britain. The only possible variable to which the author does not give much weight is that in the experimental group the parents were co-operative; in the control group the co-operation was poor.] *D. Robertson-Ritchie*

The Advance of Medicine in the Forties of the Nineteenth Century (with an index of Publications by H. Lebert, 1813-1878). (Über den medizinische Aufschwung in den vierzigen Jahren des 19 Jahrhunderts, mit einem Verzeichnis der Werke von Hermann Lebert (1813-1878). GOLDSCHMID, E. (1949). *Gesnerus, Zurich*, **6,** 17.

Six Examples of Precocious Sexual Development. I. Studies in Diagnosis and Pathogenesis. SECKEL, H. P. G., SCOTT, W. W., and BENDITT, E. P. (1949). *Amer. J. Dis. Child.*, **78,** 484.

An Influenza A Epidemic, 1947. PHELPS, E. T., and VOORHEES, W. D. (1949). *Med. Ann. Distr. Columbia*, **18,** 465.

The Rh Factor in the American Negro. A Preliminary Report. SANTOS, P. M., and STEPTO, R. C. (1949). *Amer. J. Obstet. Gynec.*, **58,** 579.

Iso-immunization by Blood-group Factors A and B in Man. HUBINONT, P. O. (1949). *Brit. med. J.*, **2,** 574.

Enlightened Eighteenth Century Views of the Alcohol Problem. HIRSH, J. (1949). *J. Hist. Med.*, **4,** 230.

Population and Polygamy in Eighteenth-century Thought. ALDRIDGE, A. O. (1949). *J. Hist. Med.*, **4,** 129.

GENERAL ADVISORY BOARD

The Editors of the *British Journal of Social Medicine* are anxious to keep in close touch with centres of social medicine in other parts of the world. To this end they are forming a General Advisory Board. The Editors note with pleasure that the following have already expressed their willingness to serve:

Dr. C. J. Brenkman (Joint Editor of the *Tijdschrift voor Sociale Geneeskunde*).

Dr. L. Derobert (*Archives de Médecine Sociale*, Paris).

Prof. Gunnar Dahlberg (Swedish State Institute for Human Genetics and Race Biology).

Sir Raphael Cilento (Director of Health and Medical Services for Queensland, and Professor of Social Medicine, Brisbane).

Dr. Karl Evang (Director General of Public Health, Norway).

Prof. Elena Fambri (Institute of Social Medicine, Rome).

Prof. M. Kacprzak (Government School of Hygiene, Warsaw).

Prof. J. Leclercq (Institute of Forensic and Social Medicine, University of Lille).

Dr. M. G. Neurdenburg (Joint Editor of the *Tijdschrift voor Sociale Geneeskunde*).

Dr. V. J. Prosek (Institute of Social Medicine, Charles University, Prague).

Prof. J. G. Remijnse (Institute of Social Medicine, University of Utrecht).

Prof. Knud Sand (President of the International Academy of Forensic and Social Medicine; Institute of Social Medicine, Copenhagen).

Prof. Réné Sand (Institute of Social Medicine, University of Brussels).

Dr. Henry E. Sigerist (Retired).

Dr. A. Stampar (Department of Public Health and Social Medicine, Zagreb University, Yugoslavia).

Prof. Wilson M. Wing (School of Hygiene and Public Health, The Johns Hopkins University, Baltimore).